NEUROPHYSIOLOGICAL RESEARCH SUPPORTING THE INVESTIGATION OF ADAPTIVE NETWORK ARCHITECTURES

CHARLES D. WOODY, M.D.
Professor of Anatomy, Psychiatry,
and Biobehavioral Science
UCLA Medical Center
Los Angeles, California
90024

Final Scientific Report

May 1985

AFOSR Contract F49620-83-C-0077

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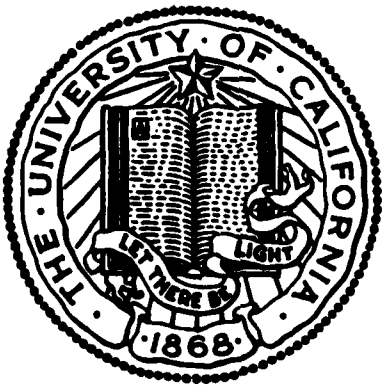

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1a REPORT SECURITY CLASSIFICATION: UNCLASSIFIED	1b RESTRICTIVE MARKINGS
2a SECURITY CLASSIFICATION AUTHORITY	3 DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution unlimited.
2b DECLASSIFICATION/DOWNGRADING SCHEDULE	
4 PERFORMING ORGANIZATION REPORT NUMBER(S)	5 MONITORING ORGANIZATION REPORT NUMBER(S): AFOSR-TR- 86-0083
6a NAME OF PERFORMING ORGANIZATION: UCLA Medical Center Dept of Anatomy	6b OFFICE SYMBOL (If applicable)
6c ADDRESS (City, State and ZIP Code): Los Angeles. CA 90024	7a NAME OF MONITORING ORGANIZATION: Air Force Office of Scientific Research/NL
	7b ADDRESS (City, State and ZIP Code): Building 410 Bolling AFB, DC 20332-6448
8a NAME OF FUNDING/SPONSORING ORGANIZATION: AFOSR	8b. OFFICE SYMBOL (If applicable): NL
	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER: F49620-83-C-0077
8c. ADDRESS (City, State and ZIP Code): Building 410 Bolling AFB DC 20332-6448	10. SOURCE OF FUNDING NOS.

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT NO.
61102F	2312	A1	A

11. TITLE: Neurophysiological Research Supporting the Investigation of Adaptive Network Architectures

12. PERSONAL AUTHOR(S): Dr Charles D Woody

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Yr., Mo., Day)	15. PAGE COUNT
Final	FROM 01 Mar 83 TO 28 Feb 85	14 August 1985	88

16. SUPPLEMENTARY NOTATION

17 COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB. GR	

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

The investigators have shown that single coritcal neurons adapt in such a way as to support learned behavior. What is particularly interesting is the indication that purposefully complex, molecular cascades exist at the level of single nerve cells to permit successful adaptions to occur. Successful adaptions are defined as: (a) producing the desired alteration of response to the appropriate input, (b) enduring over time, (c) not interfering with other adaptions occuring for other purposes in the same cell, and (d) not interfering with the main-throughput-message transfer property of the nerve cell. The result of these adaptations is to support the operation of a self-organizing information processing system with a high success: error ratio and excellent survivability in the face of substantial environmental change. Changes in the excitability of cortical neurons occur that lead to acquisition of the ability to perform specific motor tasks in response to specific auditory stimuli. Rates of acquiring this ability can be substantially increased by adding ele tric stimulation of the hypothalamus, associatively, to presentations of conventional conditioned

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21 ABSTRACT SECURITY CLASSIFICATION
UNCLASSIFIED/UNLIMITED X SAME AS RPT X DTIC USERS	UNCLASSIFIED

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE NUMBER (Include Area Code)	22c. OFFICE SYMBOL
Dr William O Berry	(202) 767-5021	NL

DD FORM 1473, 83 APR EDITION OF 1 JAN 73 IS OBSOLETE.

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SECURITY CLASSIFICATION OF THIS PAGE UNCLASSIFIED

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and unconditioned stimuli. Part of this acceleration of learning the motor response may derive from recruitment of a new performance pathway-reflected in a longer transmission latency for movement production. A long range goal of the research is to understand how the system picks the right pathway to give both acceleration and the appropriate learned movement.

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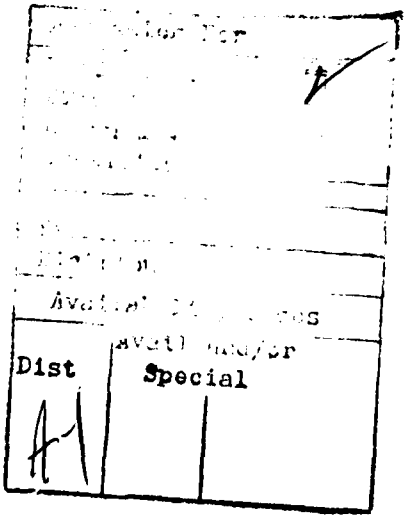
*The experiments reported herein were conducted according to the principles described in Guide for the Care and Use of Laboratory Animals DHEW Publication (NIH) 78-23.



I. SUMMARY

The human brain is the most powerful adaptive network known to man. It is responsible for human intelligence with operations involving automated image recognition, speech, decision making and complex motor functions. The same functions are the goal of artificial intelligence operations, robotics and the like. Attempts to design machines to perform these functions successfully would benefit from an understanding of how the brain has succeeded in doing so.

Both brain and machine depend on component operations. In the brain the basic component is the neuron. Although little, as yet, is known of the rules by which adaptive neural changes are brought about, experimental studies over the past 15 years have uncovered direct evidence that such changes occur and can be studied at the level of single nerve cells in the mammalian brain and in simpler invertebrate systems (Alkon, 1979, 1980a,b, 1982; Carew et al., 1983; Kandel, 1976; Kandel and Spencer, 1968; Woody, 1974, 1977b, 1982a,b; Woody and Black-Cleworth, 1973).

Our studies have shown that single cortical neurons adapt in such a way as to support learned behavior. What is particularly interesting to us is the indication that purposefully complex, "lock and key" molecular cascades exist at the level of single nerve cells to permit "successful" adaptations to occur. "Successful" adaptations are defined as: (a) producing the desired alteration of response to the appropriate input, (b) enduring over time, (c) not interfering with other adaptations occurring for other purposes in the same cell, and (d) not interfering with the main - throughput - message transfer property of the nerve cell. The result of these adaptations is to support the operation of a self-organizing information processing system with a high success: error ratio and excellent survivability in the face of substantial environmental change.

The nerve network and elements that were studied reflect a much different design from that found in single elements of most artificial information processing devices. Nonetheless, the design seems understandable in terms of conventional information processing theory and in terms of conventional systems analysis approaches. (For a brief summary of the latter see the enclosed Appendix excerpted from a recent book of mine.)

Some of the complexities of these nerve cell adaptive operations are exemplified by:

(a) A conductance <u>decrease</u> IPSP that we have found after PT stimulation (this mechanism for altering neural excitability works in just the opposite way from classical conductance increase mechanisms of PSP generation),

(b) The fact that both a strong depolarization signal <u>and</u> the availability of a calcium-activated protein kinase are needed to initiate membrane responses to the latter agent measured in cortical neurons.

We think that we are now catching "glimpses" of some surprisingly sophisticated ways in which cortical neurons adapt to support a whole range of newly learned tasks, accomplishing the task at hand while maintaining the

potential for accomplishing others. Changes in the excitability of cortical neurons occur that lead to acquisition of the ability to perform specific motor tasks in response to specific auditory stimuli. Rates of acquiring this ability can be substantially increased by adding electrical stimulation of the hypothalamus, associatively, to presentations of conventional conditioned and unconditioned stimuli. Part of this acceleration of learning the motor response may derive from recruitment of a new performance pathway - reflected in a longer transmission latency for movement production. A long range goal of our research is to understand how the system picks the "right" pathway to give both acceleration and the "appropriate" learned movement.

II. STATEMENT OF WORK

Postsynaptic neural responses to stimulation of the pyramidal tract and the hypothalamus were studied in conjunction with responses to putative transmitters and second messengers thought to contribute to development of conditioned behavior and acceleration of the rate of acquisition of conditioned behavior. Details are given in the progress report that follows.

Sixteen publications have resulted from research in the two year period of this contract; see list of publications - Part IV.

III. COMPREHENSIVE PROGRESS REPORT - STATUS OF RESEARCH

May 1983 - May 1985

1. The rate of learning a conditioned facial movement was greatly accelerated by adding electrical stimulation of the hypothalamic region of the brain to presentations of conventional conditioned and unconditioned stimuli. Animals learned the CR after as few as ten instead of 1,000 or more pairings. The learning that resulted was both associative and discriminative (Kim, Woody and Berthier, J. Neurophysiol., 1983). That is, learning was induced by a specific stimulus combination, the code depending on the order and interval of presentation of the involved stimuli. The learned response was then elicitable by a specific input signal. The pattern of cortical neuronal activity produced by hypothalamic stimulation was predictive of loci of hypothalamic stimulation that, when stimulated, would succeed in accelerating learning (Woody, Kim, and Berthier, J. Neurophysiol., 1983). Further details are available below (p. 18 ff.). Part of the acceleration of learning the motor response may derive from recruitment of a new performance pathway - reflected by a longer transmission latency for movement production. If so, one would like to know how the system picks the "right" pathway to give both acceleration and the "appropriate" learned movement. We would also like to know whether the hypothalamic stimulation responsible for acceleration of learning is punishing or rewarding. This may, however, be of less consequence in understanding what is going on than would specifying the coded molecular interactions that occur between the chemical(s) released by hypothalamic stimulation and other chemicals capable of modifying the transfer properties of the nerve cells. It is these interactions that we think are primary in controlling the potentiation of conditioning that we have observed.

2. Effects of L-Glutamate and L-Glutamic Acid Diethyl Ester (GDEE) were studied in neurons of the motor cortex that responded with short-latency discharge to hypothalamic stimulation. (Short-latency activation of these neurons by hypothalamic stimulation was predictive of loci of stimulation within the hypothalamus that could accelerate rates of acquisition of the facial CRs described above.) Extracellular recordings of unit activity were made from cells of the motor cortex of awake cats during extracellular iontophoresis of 1 M monosodium glutamate. Twenty four of the cells (86%) showed an increased firing rate in response to application of glutamate. Eight cells that demonstrated short-latency (less than 20 msec) activation in response to hypothalamic electrical stimulation were tested with iontophoretic application of glutamate. Seven of these cells showed an increased firing rate in response to glutamate. Six of these cells were then tested with hypothalamic stimulation after extracellular iontophoretic application of 0.5 M GDEE (a glutamate blocker). The short-latency response to hypothalamic stimulation was suppressed in four and reduced in one of these cells. These findings, though preliminary in number, suggest that some cells of the motor cortex that respond to hypothalamic stimulation can be activated by glutamate and that the short-latency response to hypothalamic stimulation can be suppressed by extracellular application of a glutamate blocker. Glutamate or some of its chemical analogues such as N-acetyl-aspartyl-glutamate or N-methyl-D-aspartate may be involved in the mechanism supporting accelerated rates of conditioning. (Cooper and Woody, Soc. Neurosci. Abstr., 9:330, 1983)

3. Because of the above findings, attempts were made to condition increased activity to click in single cortical neurons of awake cats using glabella tap and iontophoretically applied glutamate. (Woody, Oomura, et al, Soc. Neurosci. Abst., 1984.) Averages of click-evoked activity were compiled from single units (n = 104) of the motor cortex before and after ten serial presentations of click plus glutamate (c + g), click plus glabella tap plus glutamate (c + t + g), glutamate plus click plus glabella tap (g + c + t) and, in other cells (n = 20), after click plus glabella tap plus chloride (c + t + Cl^-). Unit activity was recorded through the same electrodes used to apply 0.5 M glutamate or 1.5 M Cl^- extracellularly (90nA, 300 ms). Mean peak responses to click $\geq$ 3 sd above mean baseline levels of activity were found only during the initial ten click presentations and after the ten presentations of c + t + g. Some units responsive to click could be found within each group of cells tested. Among the responsive cells, responses to the ten "test" clicks were largest after presentation of c + t + g, with or without subtraction of mutual baseline activity. All but one of the cells responding after c + t + g showed increased activity in response to glutamate. Our results show that application of glutamate after click-CS and tap-US can produce effects on cellular activity resembling those found after adding HS to the same CS and US. This evidence also favors the hypothesis that glutamate or a glutamate-like chemical is released at these cortical neurons by HS and that the resulting increase in activity contributes in some way to the rapidity of conditioning.

4. Depolarization-induced effects of intracellularly applied calcium-calmodulin-dependent protein kinase were studied in neurons of the motor cortex of awake cats. Intracellular iontophoretic application of calcium-calmodulin-dependent protein kinase (CaPK) was followed by a 30 sec period of steady depolarization (1.0 nA). These cells showed an increase in input resistance in comparison with a control group of fifteen cells given depolarization only, without application of CaPK (Fig. 1). Post-iontophoretic measurements of input resistance in cells given CaPK alone were not increased, nor was input resistance increased in cells given equivalent negative currents through electrodes containing only KCl. A detailed comparison of results in experimental and control neuronal populations is given in Fig. 1. The results indicate that intracellular injection of calcium-calmodulin-dependent protein kinase, followed by depolarization and depolarization-elicited impulse activity, transiently increases input resistance of neurons of the motor cortex of cats. Depolarization-induced discharge was needed to change the membrane response of cortical neurons to acetylcholine or cyclic GMP from a transient to a persistent one (cf., Woody et al., 1978). An analogous increase of input resistance can be produced in the Type B photoreceptor of Hermissenda by applying protein kinase and sufficient depolarization paired with light to increase calcium conductance and internal calcium concentration. It appears that some of the same control mechanisms responsible for elaboration of associatively induced behavioral changes in Hermissenda may be operative in neurons of the cat motor cortex that support the performance of the learned motor tasks that we are studying (Woody, Alkon and Hay, Brain Res., 1984).

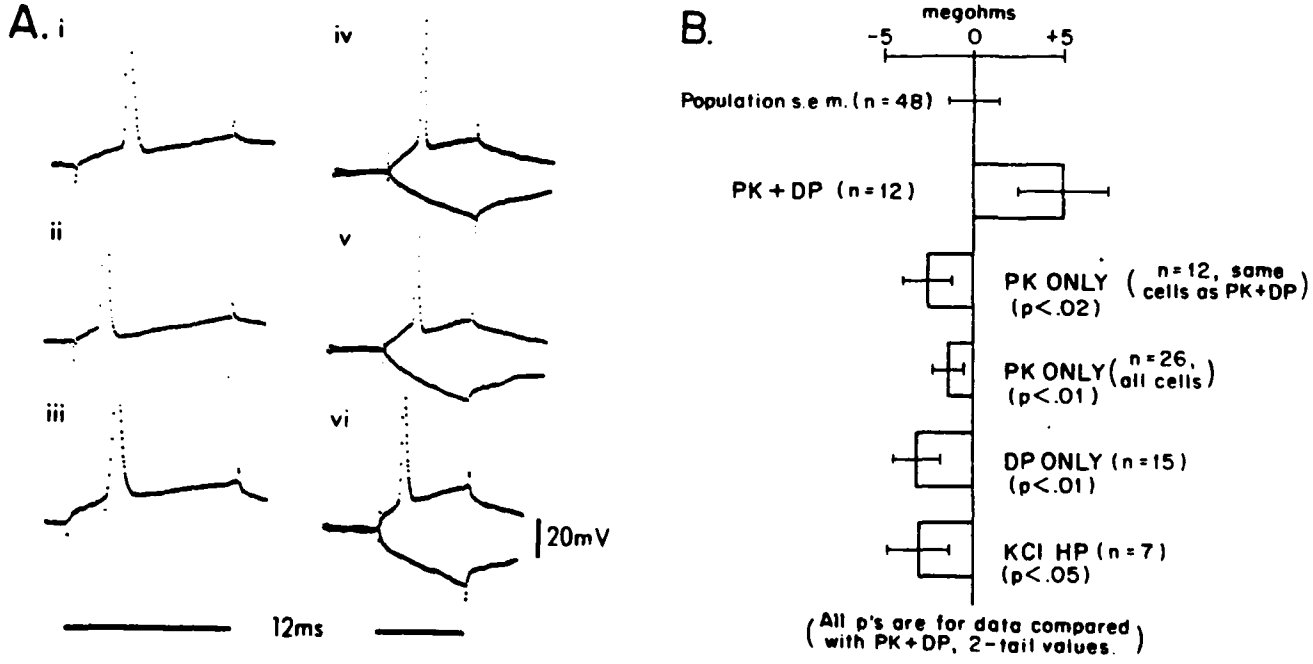


Figure 1. A) Results of intracellular injection of Ca^{2+}-calmodulin-dependent protein kinase (Ca^{2+}-CAMdPK) followed by application of depolarizing current. Input resistance: (i and iv) = before protein kinase injection; (ii and v) = after protein kinase injection; (iii and vi) = immediately after subsequent depolarization. (i, ii, and iii) show the maintenance of bridge balance to null out changes in electrode resistance. In A (ii) the bridge is slightly out of balance. An increase in resistance is seen in iii and vi. Calibrations are as indicated below and to the right of this portion of the figure. 12 ms applies to both time calibrations and the 20 mV calibration applies to all records. (The tops of the spikes are cut off.) B) Bar graphs of average change in input resistance before and after protein kinase plus depolarization in responsive cells (PK + DP), after protein kinase only (PK only), after depolarization alone (DP only), and after passage of negative current, i.e., hyperpolarization, without iontophoresis of protein kinase (KCl HP). Standard errors of the means are shown for each different group of cells.

5. Anatomical and physiological studies of intracellularly recorded neurons of the motor cortex of conscious cats were made in conjunction with intracellular injections of HRP (e.g., Fig. 2). Stable recordings characterized by action potentials of amplitudes smaller than the recorded resting potentials were correlated with recoveries of injected dendrites. Penetrations with dendritic recoveries had higher input resistances than did those with recoveries of both somas and dendrites. Increases in spike height during pressure injection were greater in recordings with dendritic recoveries than in recordings with recoveries of both somata and dendritic processes (Woody et al., J. Neurophysiol., 1984).

Additional studies assessed possible injury arising from cell penetrations. The response of penetrated neurons to repeated click stimuli was compared with that of unpenetrated (extracellularly recorded) units of the same cortical region. Responses obtained from penetrated neurons were separated into 4 groups according to the size of the recorded action potential. The magnitude of the response to click was much the same in cells with action potentials ranging between 50 - 60 mV, 40 - 50mV, and 30 - 40 mV. The magnitude was slightly greater in the group with action potentials ranging between 20 - 30 mV (suggesting some slight depolarizing injury to some of these cells). The response profiles were comparable to those of extracellularly recorded units (Woody et al., J. Neurophysiol., 1970; Woody and Engel, J. Neurophysiol., 1972). Studies using K+ ion sensitive microelectrodes indicated that "intracellular" recordings were in fact made intracellularly. It appears that whatever injury arose from the penetrations of these cells was minimal and was not sufficient to impair the ability of most cells to respond with spike activation to natural stimuli such as weak click (Woody et al., J. Neurophysiol., 1984).

6. Effects of local increases in membrane resistance on current spread in cortical pyramidal cell dendrites were explored using a passive cable model for determining the transient potential in a dendritic tree of known geometry. The morphology was obtained from a montage composed of photomicrographs taken at different, overlapping areas within serial sections of an HRP-injected, layer V pyramidal cell of the cat motor cortex. A passive cable model which could determine the transient potential in dendritic trees of arbitrary geometry was used to examine the efficacy of different loci of increased membrane resistance for given loci of current injection. The model used the passive cable equation (cf., Rall, 1962) to express the potential for each interbranch segment of the dendritic tree. By matching boundary conditions at branch points and terminations, a system of equations was readily obtained for the Laplace transform of the potential at the ends of each segment. The inverse transform could then be quickly computed for any arbitrary time point. Since only one equation was required for each interbranch segment, this approach used far fewer equations than the compartmental approach. Using this model it was found that an increase in membrane resistance in the region immediately proximal to the point of current input was more effective in increasing soma potential than an increase in a comparable membrane area of a more proximal dendritic region. Under certain circumstances a distal increase in membrane resistance could be more effective than a comparable proximal increase depending on the locus of current injection and the morphology of the dendritic tree. Tests with this model support the view that increases in membrane resistance could produce the increases in neural excitability found in these cells after conditioning and could account for the increase in activity of these neurons in response to the auditory CS (Holmes and

Woody, Soc. Neurosci. Abstr., 1983, 1984).

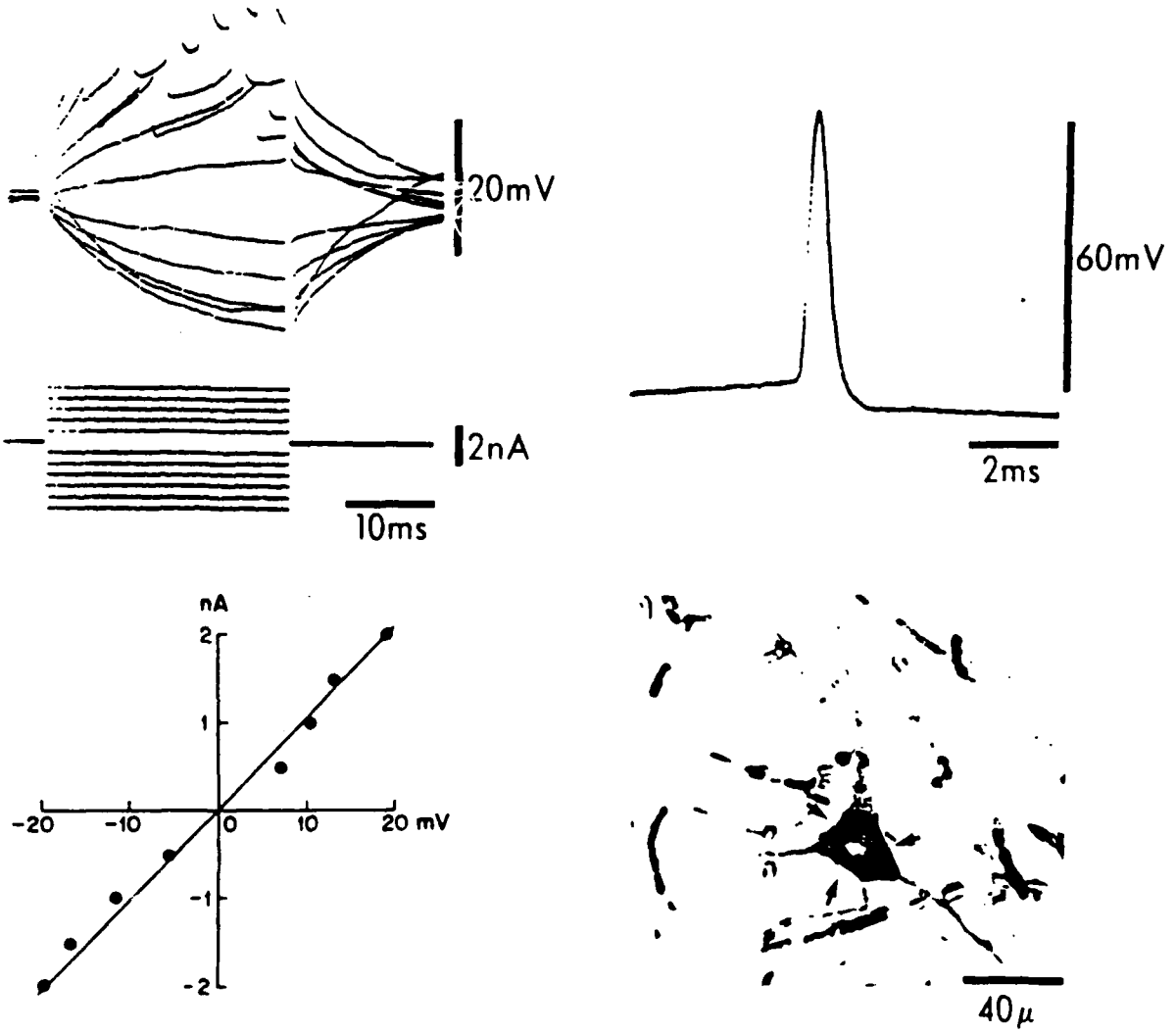


Figure 2. Electrophysiological data obtained in vivo from the HRP-injected pyramidal cell shown to the lower right. Tops of spikes elicited by depolarizing pulses are cut off.

7. Current-voltage relationships of pericruciate cortical neurons of awake cats were studied in vivo. Current pulses ranging from ± 4nA and of 30-500 ms duration were injected in 17 pericruciate neurons in order to investigate their current-voltage relationships. An active bridge circuit was used to inject the current pulses. It was important that the circuit be accurately balanced so that the measurements would not be distorted by changing electrode resistance. Therefore, an algorithm based on the method of Takeuchi et al., 1981, was used to balance the bridge circuit automatically. It required only that the electrode time constant be much shorter than the cell time constant. Current monitor and intracellular voltage records were A/D converted and analyzed (using a threshold detection method) to determine the time of current pulse onset and offset. The intracellular voltage record was sampled just before pulse onset and just after charging of the electrode (i.e., about 50-100 usec after pulse onset), the difference in the two measurements being the magnitude of bridge imbalance. This difference was then subtracted from the voltage trace for the duration of the current step, and the data D/A converted and displayed oscillographically. The slope of the IV plot in the hyperpolarizing region was taken as the best estimate of input resistance. It averaged 9.1 megohms across the 17 neurons. The cells had a mean resting potential of 62 mV, and a mean action potential height of 59.6 mV. Rectification was not detectable in the range of ± 0.5 nA current injection in 94% of the cells (Berthier and Woody, Soc. Neurosci. Abstr., 1983).

8. Effects of PT stimulation on PSP production were studied in intracellular recordings from 62 cells of the motor cortex of awake cats. (Woody, et al, Brain Res., 1985). Of these cells, 10 showed an IPSP that decreased with hyperpolarization and, in 5 of the 10 cells, the IPSP was reversed with additional hyperpolarizing current. In 9 of the cells, it was possible to measure a decrease in resistance at the time of the IPSP. This IPSP has been recognized previously by other investigators and is thought to reflect an increase in chloride conductance. In 30 of the remaining cells, a quite different IPSP was found during the same 35-120 msec period following PT stimulation. In each of these cells, the IPSP increased in size with the application of hyperpolarizing current and could not be reversed with hyperpolarization. With depolarizing current the IPSP decreased in size. The resistance was measured at the time of the IPSP by comparing the magnitude of a continuously repeated (20 ms on, 20 msec off) bridge pulse during the IPSP with that prior to the PT shock that elicited the IPSP. An increased resistance was found to accompany the IPSP. Conductance decrease IPSPs were seen in these cells irrespective of whether antidromic spikes were produced by PT stimulation. Conductance decrease IPSPs have been reported previously (Siggins et al, 1971; Engberg and Marshall, 1971; Smith and Weight, 1977), but not in neurons of the motor cortex. (PT stimulation is an effective US in producing conditioned behavior [O'Brien et al., 1977].)

9. Cybernetic considerations relevant to a theoretical approach to analysis of neuronal adaptation in a nerve network, excerpted from a book on Memory, Learning, and Higher Function by Dr. Woody, are enclosed as an Appendix. Some aspects of that material may be summarized as follows:

An adaptive system can be described, cybernetically, as a system that modifies its internal structure as a function of experience, thereby altering the system operation. Ordinarily, the system operation will become increasingly optimized, by means of feedback, in the approach to some operational goal. In this context goal-seeking will be the process by which the component or adaptive element moves toward or maintains a particular system state. A key feature of any adaptive system will be the features controlling the adaptation. The control sub-system may or may not require associated memory. If so, the memory may evolve in a trivial or non-trivial fashion, with or without variation in the original set point. Control of goal-seeking may be expected to be accomplished by means of feedback. The latter will ordinarily involve some closed-loop operations. Interestingly, a great many psychophysiological formulations of adaptive neural systems have neglected to specify closed-loop operations by which such feedback could be accomplished as opposed to open-loop operations which do not lend themselves to modification of the involved element as a consequence of the element's past adaptation (cf., Kandel and Spencer, 1968).

Physiologically, many adaptive cellular systems lend themselves to closed-loop goal-seeking processes. These range from biochemical feedback loops (within the metabolic context of the cell itself) to recurrent collateral systems with relatively direct feedback as well as indirect feedback through more extensive polysynaptic networks (cf., Rasmussen and Goodman, 1977; Phillips, 1974). At the level of cellular components in the brain, there exist several candidate mechanisms for the control of neural adaptation:

i) The "Yin-Yang" hypothesis has been advanced in which so-called excitatory and inhibitory neurotransmitters could control closed-loop goal-seeking adaptations depending upon neuronal conductance changes by means of intracellular second messengers such as cyclic AMP and cyclic GMP. The cyclic nucleotides are thought to interact reciprocally to facilitate either excitatory or inhibitory effects (Bloom, 1975, 1976; Goldberg et al., 1973).

ii) The principle of voltage-dependent control of neuronal spike activity is well established. The possibility arises of voltage dependent induction or potentiation of cyclic nucleotide release as well as the likelihood of coupled sodium or potassium-calcium channels with voltage-dependent features (Loewenstein, 1975; Lux and Eckert, 1974; Heyer and Lux, 1976a,b).

iii) Entrainment, i.e., the production of multiple spike discharges encroaching upon relative refractory periods, might furnish a chemical signal for cellular mechanisms controlling neural adaptation, particularly after associative stimulus pairings as in conditioning. In cortical neurons, entrainment is probabilistically an uncommon event in contrast with PSP or spike production, per se, resulting from natural auditory stimuli which serve as CS's in Pavlovian blink conditioning (Woody et al., 1970; Engel and Woody, 1972). Other evidence (Woody et al., 1976) indicates that entrainment might interact with acetylcholine or cyclic GMP to control aspects of

persistent adaptation in mammalian cortical neurons.

The practical significance of using a closed-loop cybernetic approach to understand cellular adaptation, even at the biochemical level, is just beginning to be re-evaluated and appreciated. For example, the following is excerpted from a review article by Rasmussen and Goodman (1977).

B. Open-Loop vs. Closed-Loop Control Systems

1. General features

Nearly all models of peptide and amino hormone action, including the second-messenger model, have been ones in which a stimulus (the hormone) acts on a particular cell or subcellular system to produce a physiological response. In cybernetic terms, this is defined as an open-loop system (Fig. 2).

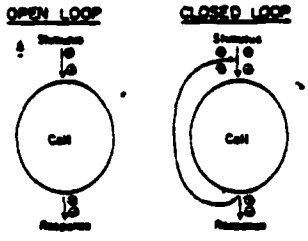


FIG. 2. Schematic representations of the contrast between open-loop and closed-loop systems in the control of cellular responses.

However, in biological systems at all levels of organization, responses are dependent not only on present and past stimuli but on the response itself, according to the present organization of the unit and its particular environment. This means that cellular responses to hormonal stimuli operate not as open- but as closed-loop systems. The distinction is critically important: in an open-loop system the response depends on the stimulus, but the converse is not true. In contrast, in a closed-loop system the response influences the stimulus—i.e., there is a feedback relationship between stimulus and response such that the response itself modifies the effect and magnitude of the original stimulus. Endocrine physiologists have realized for years that at the supracellular level endocrine systems operate as complex, closed-loop systems (327), yet most endocrine biochemists continue to analyze hormone action at the cellular level in the context of open-loop models (128, 190, 415).

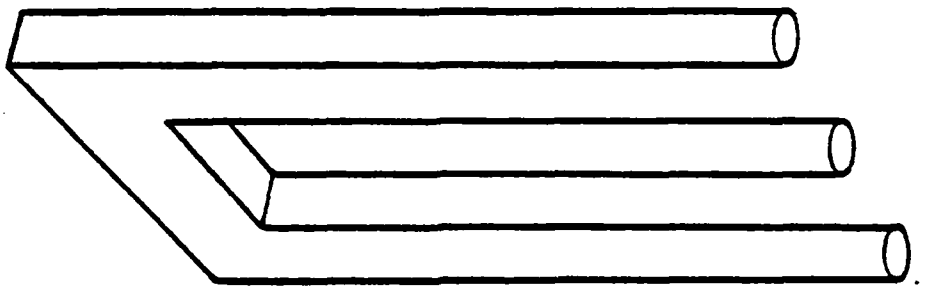
Considering these cellular control systems as closed-loop systems as schematized in Figure 2, rather than an open-loop yin-yang system as proposed by Goldberg et al. (163), adds an important dimension to both one's understanding of the system and to the types of critical experiments one can design to evaluate the hypothesis.

The importance of making this distinction in analyzing hormone action lies in the kinds of models of hormone action one builds from experimental data and from these the type of further experiments one designs to test these models. Of even greater import, if closed-loop systems are the biological rule, then an understanding of feedback theory provides a means of obtaining a correct intuitive grasp of the nature of the control system in many situations in which an open-loop analysis of the same experimental data would lead to a confusing and contradictory conclusion.

(From Physiological Reviews)

Systems of this type are of course restricted in the type of operations they can perform and the geometric patterns that can be recognized. For example, such systems cannot compute connectedness of geometric figures, whereas they can compute convexity and related processing operations of the type called local or conjunctively local by Minsky and Papert. Humans may not be able to compute some forms of connectedness either:

e.g.:



The possibility exists that modification of Uttley's algorithm can result in the introduction of a <u>self-classifying</u> input. By self-classifying input is meant an input of particular functional significance which is identifiable, within the adaptive element, by means of its stochastic pattern of appearance alone. Moreover, this stochastic pattern need not unduly disrupt the overall function of the adaptive element's operation.

The informon model of an adaptive neural element (Uttley, 1976) incorporates classifying inputs, closed-loop feedback concerning the operational state of the element, and an appreciation of goal-seeking in the algorithm regulating useful adaptation. Several constraints are particularized that are critical if the informon is to successfully discriminate one input from another. These are a) the algorithm by which the weightings of synaptic inputs are altered, b) the need to achieve system normalization through negative (not positive) feedback of information regarding the current system state, and c) the need for a classifying input to distinguish or identify which input signal is the particular signal to be discriminated. Tests of this model have found that each of these constraints is required for the element to adapt usefully. Synaptic weighting is altered according to the Shannon mutual information function between certain synaptic inputs in combination with closed-loop negative feedback reflecting the element's internal state. In summary, it would appear that there are empirical as well as theoretical reasons why "smart" adaptive elements need to incorporate goal-seeking as well as closed-loop feedback into their design.

In some adaptive networks, input analysis, i.e., the processing of sensory-labelled information (cf., Mountcastle, 1974), is explicable in terms of the group invariance theorem of Minsky and Papert. This theorem permits analysis of operations, such as the geopmetry of certain sensory image processing, by algebraic means instead of statistics and thereby reverses a trend in this field. The group invariance theorem examines the relationship

between all possible receptor activations (all sets of sensory labels) and their representation across the theoretical space of an adaptive network, given certain architectural constraints. This result is a description of an orderly relationship in which no matter how complexly the network is organized, the space required for a particular sensory labelling can be specified. In summary form, the group invariance theorem states that if:

i) G is a finite group of transformations of a finite space R;

ii) $\underline{\Phi}$ is a set of predicates on R closed under G;

iii) ψ is in L ($\underline{\Phi}$) and invariant under G.

Then there exists a linear representation of

$$\psi = \left[\Sigma_{\varphi \in \underline{\Phi}} \beta_\varphi \varphi > 0\right]$$

for which the coefficients β_φ depend only on the G-equivalence class of φ, that is if $\varphi \underset{G}{=} \varphi'$ then $\beta_\varphi = \beta_{\varphi'}$.

L $\underline{\Phi}$ is the set of all predicates for which ψ is a linear threshold function with respect to $\underline{\Phi}$, and a predicate is a function that has two possible values, i.e. a binary function.

ψ is a linear threshold function with respect to $\underline{\Phi}$ (ψ is in L ($\underline{\Phi}$)), if there exists a number θ, and a set of numbers, α_φ one for each φ in $\underline{\Phi}$, such that:

Equation 2.6

$$\psi(x) = \left[\Sigma_{\varphi \in \underline{\Phi}} \alpha_\varphi \varphi(x) > \theta\right] ?$$

Research supported by AFOSR (1978-1982)

1. The sampling distribution of neurons obtained by our intracellular, cortical recording procedure was investigated. The sample of HRP-identified neurons was found to be essentially equivalent to that seen in-situ (determined from Golgi-stained sections of these cortical regions). Seventy percent (70%) of penetrations were of cells in layers III and V, and 70% of the penetrations were of pyramidal shaped cells. There was a slight tendency to over-sample neurons with extensive dendritic arborizations. Samplings of every major morphologically identified in-situ neuronal type were obtained by our electrophysiological procedures (Sakai et al., Brain Res., 1978).

2. The response properties of penetrated neurons to injected polarizing currents were investigated and found to be normal. The accommodative response to ramp depolarizing currents was assessed; most responses were of the simple type rather than ceiling or minimal gradient, (cf., Koike et al., Exp. Br. Res., 1968a,b). Normal I-V plots and input resistance were also obtained. Several lines of evidence suggested that many cortical neurons have dendrites that do not support active propagation of action potentials and, instead, serve the integrative process of neuronal information handling (Woody and Gruen, Brain Res., 1978).

3. In-vitro calibrations of pressure microinjection techniques were obtained. Controlled release of 100 femtoliter volumes was demonstrated. A number of other laboratories are adopting this technique for testing local biologic effects of pharmacologic agents (cf., Sakai et al., Neuropharmacol., 1979).

4. Preliminary evaluations of effects of acetylcholine (ACh) and cyclic GMP (cGMP) on cortical neurons were completed. These agents appear to have similar effects on input resistance, ACh acting extracellularly on cell surface receptors (of muscarinic type), cGMP acting intracellularly. The input resistance is increased transiently by the effect of these agents alone and persistently by application with cell depolarization sufficient to produce repeated discharge (Woody et al., Brain Res., 1978).

It appears that neurotransmitters act in a dual manner in these cells, as in others, to convey information. One action, the direct "neurotransmitter effect", serves primarily to transmit information through the cell. The other action, the "modulatory effect", serves to control adaptation as a function of the information transmitted. The two actions are kept separated in the time-frequency domain by different time courses of involved biochemical pathways; (cf., Klopf, A.H., Brain Function and Adaptive Systems -- A Heterostatic Theory, AFCRL Dept., H133, 1972).

A third variable, depolarization included discharge, serves to make the adaptation persistent rather than transient.

5. In a simulated neuron, consequences of propagative vs. non-propagative dendritic membranes on information transfer were studied. With low rates of current spread, graded changes in threshold produced graded changes in output discharge. With high rates of current spread, the neuron became a bistable (decisional) operator where spiking was enhanced if the threshold was below a certain level and suppressed if above that level. The enhancement was considerably more pronounced in neurons with non-propagative than with propagative dendrites. With propagative dendrites a less intense input was needed to initiate somatic spiking (Levine and Woody, Biol. Cybernetics, 1978).

6. Studies of the ability to morphologically identify types of neurons responding to cholinergic agents were conducted using aceclidine, a cholinomimetic drug. Similar increases in input resistance were obtained with this drug as with ACh and the effects could be blocked by atropine (a muscarinic receptor blocker). One of the cells responding to aceclidine with an increased resistance was identified by injection of HRP as a pyramidal cell of layer VI (Swartz et al., Proc. West. Pharm. Soc., 1978).

7. Effects of acetylcholine (ACh) and cyclic GMP (cGMP) on input resistance were studied in groups of morphologically identified neurons. HRP was pressure injected into the cells after studying the effects of ACh. cGMP was also applied intracellularly by pressure injection. Pyramidal cells of layers V and VI responded to these agents with increases in resistance. The responsive neurons included those of layer V activated antidromically by PT stimulation.

A comparison of the results of pressure injected cGMP with those of intracellularly iontophoresed cGMP showed similar changes in resistance, but the increase in firing rate after the hyperpolarizing iontophoresis did not occur after pressure injection. The results suggest that cGMP and acetylcholine produce similar effects in similar neurons of the motor cortex, the primary effect being a conductance decrease. The increase in firing rate following application of acetylcholine appears to be a separate effect of this agent, apart from that supported by cGMP as a second messenger. This effect may arise from excitation of surrounding neurons presynaptic to the one recorded or from other, direct conductance effects of acetylcholine binding at the neuronal receptors. (Swartz and Woody, J. Neurobiol., 1979; Woody et al., Soc. Neurosci. Abstr., 1979).

8. Effects of low frequency PT stimulation on cortical neural excitability. Antidromic stimulation of the pyramidal tract has been used successfully as a US to produce conditioned learning (O'Brien et al., 1977). Effects of low frequency 4-6 Hz PT stimulation (stereotax. coord.: F 3.5, L 4.0, H 4.5) on cortical neurons were investigated. Cortical cells activated antidromically responded predominantly with reduced excitability to intracellularly applied current. Cortical cells activated transsynaptically responded with increased intracellular excitability. Those cells failing to respond showed no change in excitability during the 5-15 minutes tested. (Tzebelikos and Woody, Brain Res. Bull., 1979).

9. The effects of US presentations on rates of discharge and excitability to weak extracellular current were studied in single units of the motor cortex. (Brons, Woody and Allon, J. Neurophysiol., 1982). The excitability to weak (nA) extracellular electrical stimulation was measured among single neurons of the pericruciate cortex of awake cats as a function of behavioral state. Levels of neuronal excitability were compared 1) after classical conditioning of a facial movement, 2) during extinction of the conditioned response, and 3) during unpaired presentations of conditioned and unconditioned stimuli (CS and US).

Neurons projective to facial muscles via polysynaptic corticofugal pathways showed decreased levels of excitability to weak extracellular stimulation following conditioning with forward pairing of the CS and US, extinction with backward pairing of the stimuli, and presentations of the US alone. These changes in excitability were attributable solely to the effects of US presentation and were not distinguishably different during either conditioning or extinction of the behavioral response. Small decreases in rates of spontaneous firing were found to accompany the decreases in neural excitability.

The data support the conclusions that significant nonassociative changes in neural excitablility occur during conditioning and extinction due to presentations of the unconditioned stimulus. These changes support latent inhibition, behaviorally, and the mechanism of these changes is different from that of changes in postsynaptic excitability found, after conditioning, by intracellular stimulation of similiar cortical neurons (Woody, Fed. Proc., 1982). The increased excitability to intracellular currents facilitates performance of the specific type of motor response that is acquired and is also latent, awaiting a command signal that will cause the response to be initiated.

Further details about studies of rapid learning.

The rapidity of acquisition of conditioned motor responses was determined after adding hypothalamic stimulation to click CS and glabella tap US. Our analyses showed a two order-of-magnitude acceleration of the rate of acquisition of a blink response over that achieved by pairing the same CS and US without hypothalamic stimulation (Kim, Woody and Berthier, J. Neurophysiol., 1983). Changes in the patterns of activity of single units of the motor cortex were isomorphic with the development of the conditioned response (Woody, Kim and Berthier, J. Neurophysiol., 1983).

Additional findings were obtained following completion of the following computer programs.

Computer Program

The program consists of three functional units: stimulus presentation and data collection, histogram generation and display, and behavioral analysis and data storage. Conditioned (CS), unconditioned (US), hypothalamic (HS), and discriminative (DS) stimuli are presented in a timed sequence for ten second trials of adaptation, conditioning, extinction, or delayed HS paradigms. Timing of stimuli can be generated spontaneously for on line experiments or synchronized to an analog tape pulse for analysis of prerecorded data. During each trial, five seconds of EMG data encompassing all stimuli are sampled at 2 ms intervals from the left and right orbicularis oculi and levator oris. Eight histograms are generated from the data and displayed four each on Mime 100 and VT105 video terminals. The histograms are averages of three trials and are normalized to the tallest bin. The Mime 100 histograms are 400 ms displays encompassing the CS-US period for each EMG. The VT105 histograms can be dynamically modified by keyboard codes which can center histograms around any stimuli for any EMG and display from 100 to 1600 ms of data.

The computer detects conditioned EMG responses using the criteria that 3 consecutive samples in the current trial plus 1 of the 2 previous trials plus the average of those 3 trials must exceed 5 standard deviations above the mean of spontaneous activity sampled for 400 ms before the CS. The response must be detected between 100 ms after the CS and 20 ms before the US. If a response based on these criteria is found, the three trials are individually stored on disc while no response results in three trials being averaged before disc storage.

Results

The results of training cats with click CS, tap US, hypothalamic stimulation (HS), and an added hiss DS are shown in Figure 3. They indicate that, with this paradigm, discriminative responses to the CS are acquired within 9 trials. The rate of acquisition is two orders of magnitude faster then when HS is omitted and permits intracellular recording from cortical neurons while learning takes place. The latencies of the CRs range between 100 and 300 ms.

Additional effects on conditioning of adding hypothalamic stimulation (HS) to classical application of CS (click) and US (glabella tap) have also been examined:

a. Learning in animals given stimulation at effective hypothalamic loci was compared with failure to learn in animals given stimulation at ineffective hypothalamic loci. Figure 4 shows some effective and ineffective loci (Kim, Woody and Berthier, J. Neurophysiol., 1983).

b. Patterns of cortical unit response to hypothalamic stimulation may be predictive of an effective locus of hypothalamic stimulation for producing enhanced rate of learning. Patterns of activity such as those shown in Figure 5 have been seen with effective hypothalamic stimulation (Woody, Kim, and Berthier, J. Neurophysiol., 1983).

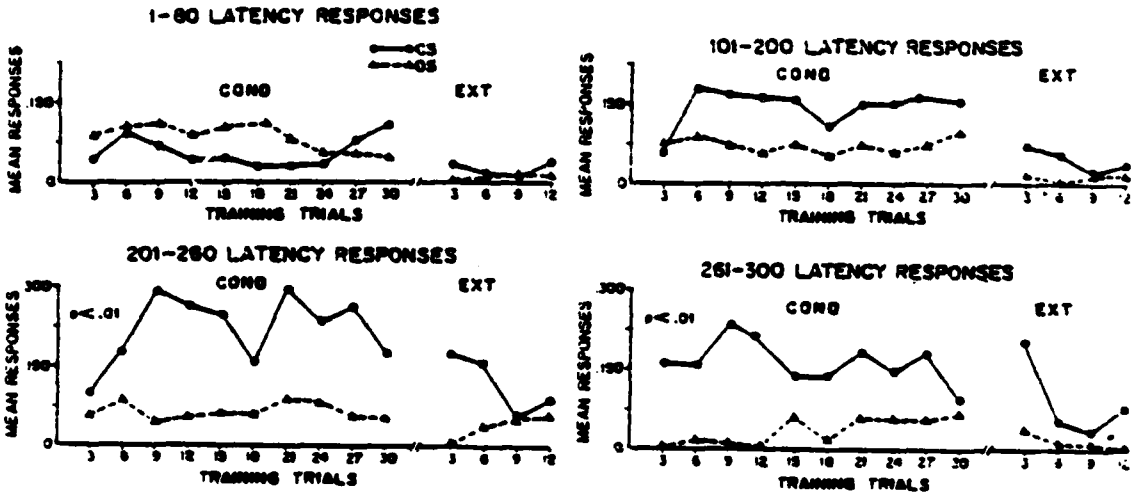


Figure 3. Rapidity of Conditioning and Latency of CR's

Development of EMG responses of different latencies to CS (Solid line) or DS (Dashed line) in 8 cats during conditioning. Responses were defined as EMG responses of greater than 5 sd above the pre-CS (spontaneous) mean. During training, CRs increased with trials reaching asymptote (74% CRs) within 9 trials. Responses were classified into four windows (0-80 ms, 101-200 ms, 201-260 ms, 261-300 ms; top to bottom, respectively). Cats made more responses to the CS than DS when responses of greater than 101 ms were analyzed. During extinction cats made more responses to the CS than to the DS, but by the ninth trial of extinction there was little responding to either the CS or DS.

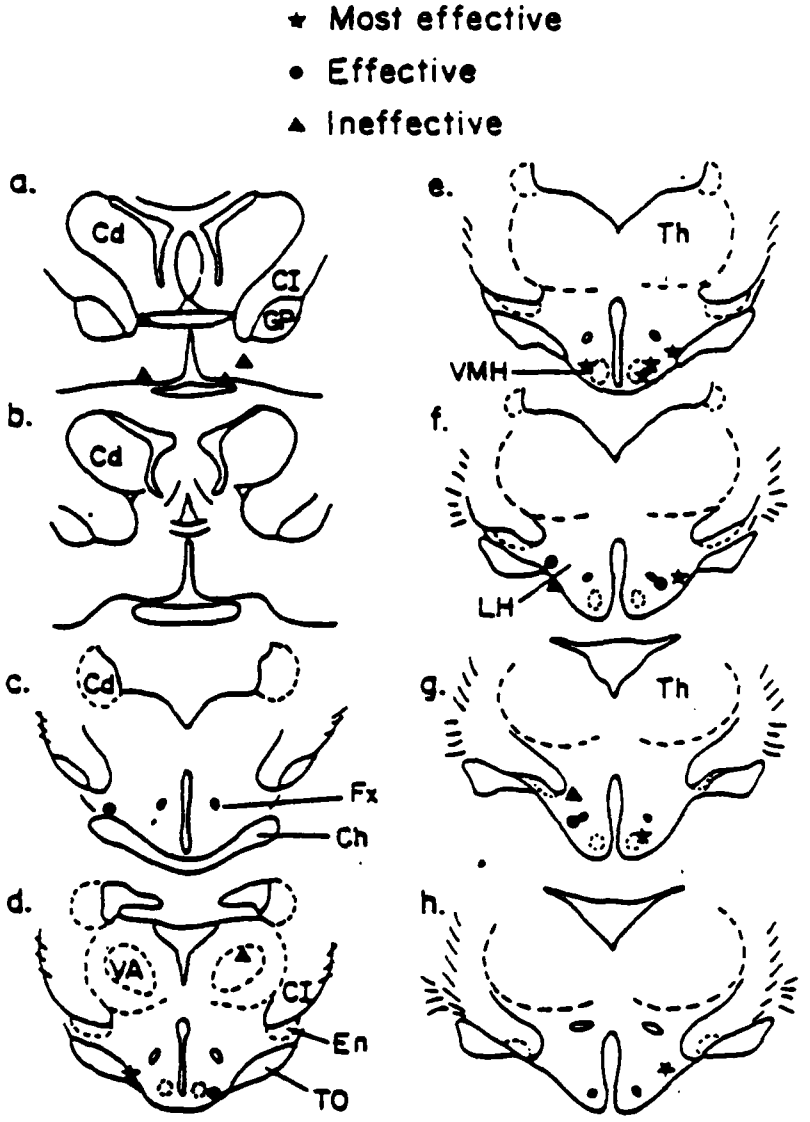


Figure 4. Loci of Brain Stimulation

Filled stars represent hypothalamic sites, stimulation of which produced rapid acquisition of discriminative eye-blink CRs at over 90% performance level. The sites of stimulation that resulted in discriminative CRs being performed less consistently are represented by filled circles. Behaviorally ineffective sites of stimulation are indicated by filled triangles.

Abbreviations: Cd, caudate nucleus; Ch, optic chiasm; CI, internal capsule; FX, fornix; GP, globus pallidus; LH, lateral hypothalamus; Th, thalamus; TO, optic tract; VMH, ventromedial hypothalamic nucleus.

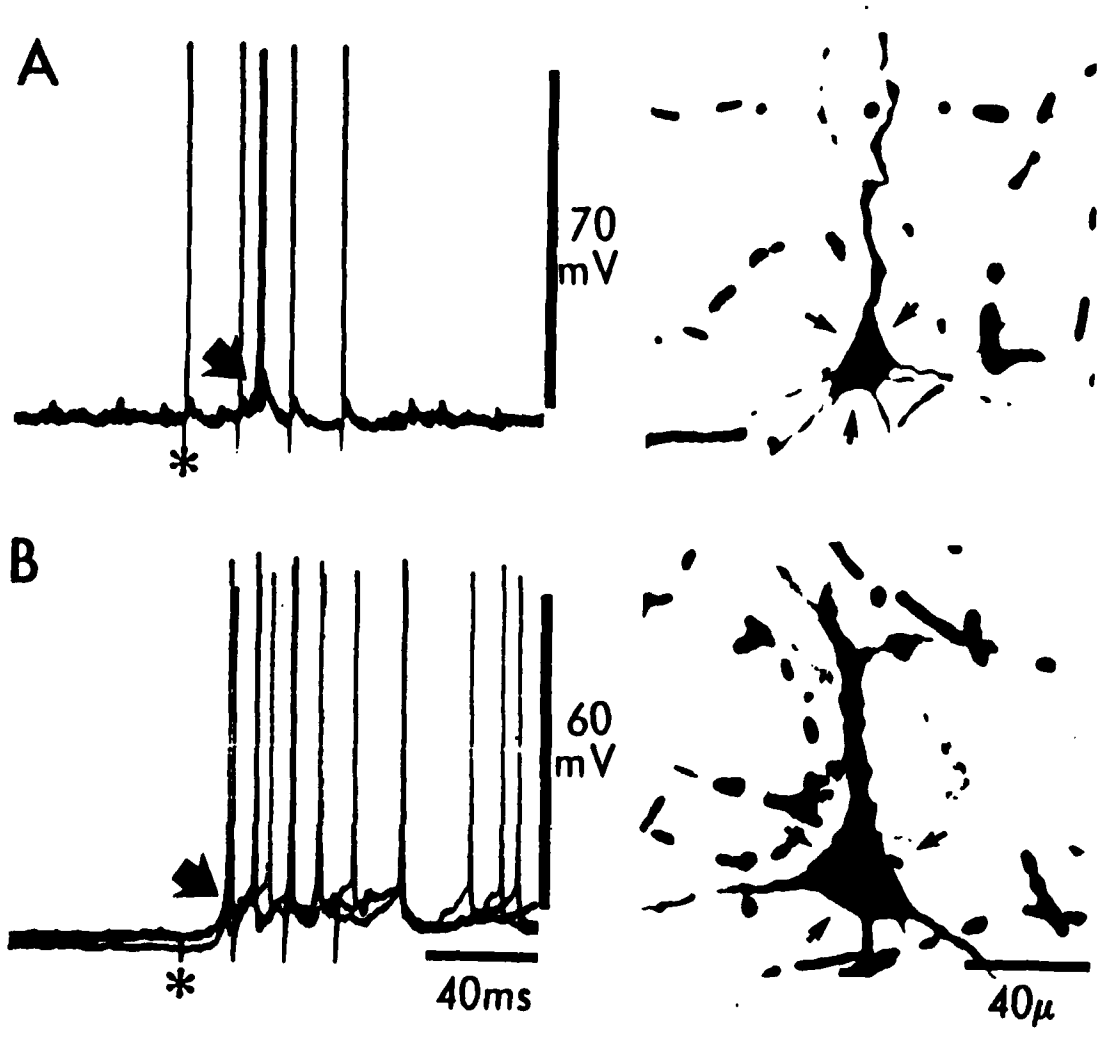


Figure 5. Responses to hypothalamic stimulation (* is first of four electrical pulses) of two (A and B) HRP-injected pyramidal cells of the cat motor-sensory cortex.

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14. Levine, D.S. and Woody, D.C. Effects of active versus passive dendritic membranes on the transfer properties of a simulated neuron. Biol. Cybernetics 31: 63-70, 1978.

15. Tzebelikos, E. and Woody, C.D. Intracellularly studied excitability changes in coronal-pericruciate neurons following low frequency stimulation of the cortobulbar tract. Brain Res. Bull. 4: 635-641, 1979.

16. Swartz, B.E. and Woody, C.D. Correlated effects of acetylcholine and cyclic guanosine monophosphate on membrane properties of mammalian neurocortical neurons. J. Neurobiol. 10: 465-488, 1979.

17. Woody, C.D., Sakai, H., Swartz, B., Sakai, M., and Gruen, E. Responses of morphologically identified mammalian, neocortical neurons to acetylcholine (ACh), aceclidine (Acec) and cyclic GMP (cGMP). Soc. Neurosci. Abstr. 5: 601, 1979.

18. Kim, H-J. and Woody, C.D. Facilitation of eye-blink conditioning by hypothalmic stimulation. Soc. Neurosci. Abstr. 5: 319, 1979.

19. Brons, J. and Woody, C.D. Changes in responsiveness to glabella tap among neurons in the sensorimotor cortex of awake cats. Soc. Neurosci. Abstr. 5: 314, 1979.

20. Sakai, H. and Woody, C.D. Identification of auditory responsive cells in the coronal-pericruciate cortex of awake cats. J. Neurophysiol. 44: 223-231, 1980.

21. Nahvi, M.J., Woody, C.D., Tzebelikos, E., and Ribak, C.E. Electrophysiological characterization of morphologically identified neurons in the cerebellar cortex of awake cats. Exp. Neurol. 67: 368-376, 1980.

22. Ribak, C.E., Woody, C.D., Nahvi, M.J., and Tzebelikos, E. Ultrastructural identification of physiologically recorded neurons in the cat cerebellum. Exp. Neurol. 67: 377-390, 1980.

23. Brons, J.F. and Woody, C.D. Long-term changes in excitability of cortical neurons after Pavlovian conditioning and extinction. J. Neurophysiol. 44: 605-615, 1980.

24. Woody, C.D. and Gruen, E. Effects of cyclic nucleotides on morphologically identified cortical neurons of cats. Proc. Int. Union Physiol. Sci. 14: 789, 1980.

25. Woody, C.D., Ribak, C.E., Sakai, M., Sakai, H., and Swartz, B. Pressure microinjection for the purposes of cell identification and subsequent ultramicroscopic analysis. In: Current Trends in Morphological Techniques, Vol. II (Ed. J.E. Johnson, Jr.), CRC Press, Inc., 1981.

26. Woody, C.D. Studies of conditioning and other forms of adaptation in the mammalian CNS, In: Cellular Analogues of Conditioning and Neural Plasticity Ed. Feher, O., and Joo, F. Advances in Physiological Science, Pergamon Press and Akademiai Kiado, Oxford, 36: 117-128, 1981.

27. Berthier, N.E., Betts, B., and Woody, C.D. Rapid conditioning of eyeblink reflex: response topography. Soc. Neurosci. Abstr. 7:750, 1981.

28. Brons, J., Woody, C.D., and Allon, N. Changes in the excitability to weak intensity electrical stimulation of units of the pericruciate cortex in cats. J. Neurophysiol. 47:377-388, 1982.

29. Woody, C.D. Acquisition of conditioned facial reflexes in the cat: cortical control of different facial movements. Fed. Proc. 41:2160-2168, 1982.

30. Berthier, N.E., Betts, B., and Woody, C.D. Discriminative conditioning of eyeblink with aversive brain stimulation. Soc. Neurosci. Abstr. 8:315, 1982.

31. Bindman, L., Woody, C.D., Gruen, E., and Betts, B. PT stimulation produces conductance IPSPs in neurons of the motor cortex of cats. Soc. Neurosci. Abstr. 8:540, 1982.

32. Wallis, R.A., Woody, C.D., and Gruen, E. Effects of intracellular pressure injections of calcium ions in morphologically identified neurons of cat motor cortex. Soc. Neurosci. Abstr. 8:909, 1982.

33. Woody, C.D. (Ed.) Conditioning: Representation of Involved Neural Functions. Plenum Press, New York, 1982.

34. Woody, C.D. Neurophysiological correlates of latent facilitation. In: Woody, C.D. (Ed.) Conditioning: Representation of Involved Neural Functions. Plenum Press, New York, 1982, pp. 233-248.

35. Woody, C.D. Memory, Learning, and Higher Function. Springer-Verlag, New York, 1982.

V. PROFESSIONAL PERSONNEL ASSOCIATED WITH THE RESEARCH EFFORT

Charles D. Woody, M.D.*

Nahum Allon, Ph.D.

Shuji Aou, M.D., Ph.D.*

Tamas Bartfai, Ph.D.

Neil E. Berthier, Ph.D.

Lynn J. Bindman, Ph.D.

Dorwin Birt, Ph.D.*

Haing-Ja Kim, Ph.D.

Michukazu Matsumura, Ph.D.

Abbreviated curriculum vitae attached.

*Current personnel

PII Redacted

CURRICULUM VITAE

Name: Charles Dillon Woody

[redacted]

Education:

1957 - A.B. Princeton University
1962 - M.D. Harvard Medical School (Magna Cum Laude)

Positions Held:

1977 -	Professor, Anatomy, Psychiatry and Biobehavioral Science, UCLA
1983 (summer)	Distinguished Visiting Professor, National Institute for Basic Biology, Okazaki, Japan
1982 (summer)	Research Scientist, Marine Biological Laboratory, Woods Hole, Massachusetts
1976 - 1977	Associate Professor in Residence of Anatomy and Psychiatry, University of California at Los Angeles
1971 - 1976	Associate Professor in Residence of Anatomy, Physiology, and Psychiatry, University of California at Los Angeles
1968 - 1971	Research Officer (permanent), Laboratory of Neural Control, NINDS, NIH, Bethesda, Maryland
1967 - 1968	Harvard Moseley Fellow with Dr. Jan Bures, Institute of Physiology, Czechoslovakian Academy of Sciences, Prague, Czechoslovakia
1964 - 1967	Research Associate, Laboratory of Neurophysiology, NIMH, NIH, Bethesda, Maryland
1963 - 1964	Research Fellow in Neurology, Harvard Medical School, Resident in Neurology, Boston City Hospital, Boston
1962 - 1963	Intern in Medicine, Strong Memorial Hospital, University of Rochester, Rochester, New York
1960 - 1961	NIH Post-sophomore Research Fellow at Stanley Cobb Laboratory, Massachusetts General Hospital, Harvard Medical School, Boston
1959 (summer)	Research Assistant, Communications Biophysics Group, Massachusetts Institute of Technology, Cambridge, Massachusetts

Honors and Fellowships:

Leon Resnick Prize for promise in research, Harvard Medical School, 1962
Moseley Fellowship (Harvard Medical School), 1967-1968
Nightingale Prize (Biol. Engng. Soc. and Internat. Fed. Med. Biol. Engng. for best paper - International Journal: Med. Biol. Engng. 1966-1968) 1969
Honorary Member, Pavlovian Institute, U.S.S.R., 1972
Representative of Society for Neuroscience to Physiological Reviews, 1974-1980
Member, Brain Research Institute, and Mental Retardation Research Center, UCLA
Member, Neuroscience Committee supervising the UCLA Medical Center Graduate Program in Neuroscience
Bing Fellowship (Natl. Acad. Sci.) - Visiting scientist to USSR and Czechoslovakia, 1972
Chairman, Session on "Brain and Behavior", FASEB Annual Meeting, 1973
Chairman, Session on "Behavior and Conditioning", International Congress of Physiological Science, New Delhi, 1974
Invited Research Scientist and Lecturer at Kyoto University Primate Center, Japan; sponsored by Japan Society for the Promotion of Science, 1975
Chairman, Session on "Behavior and Neuroethology", FASEB Annual Meeting, 1977
Invited Panelist, Session on "Association Systems and Sensorimotor Integration", International Physiological Congress, Paris, 1977
Chairman, Session on "Neurotransmitters", Soc. for Neuroscience, October, 1979.
Exchange Fellowship (National Academy of Science), Prague, 1979.
Consultant to Publications Committee, American Physiologic Society, 1980.
Grant Proposal Reviewer, NSF, NIH, ADAMHA, NIMH
Consultant Biopsychology Study Section, NIMH, 1981
Chairman, Session on "Learning and Memory", Society for Neuroscience, October, 1983
Distinguished Professor, National Institute for Basic Biology, Japan, 1983

Editorial Service and Research Consulting:

Member, Editorial Board, Physiological Reviews 1974-1980
Editor, Soviet Research Reports, UCLA Brain Information Service
Member, Editorial Board, Brain Research Bulletin
Member, Editorial Board, Neuroscience and Behav. Physiol.
Member, Board of Editorial Commentators, Current Commentary in Behavioral and Brain Sciences
Reviewer for: EEG. Clin. Neurophysiol., Physiol. Behav., J. Comp. Physiol. Psychol., Behav. Biol., J. Neurophysiol., Exper. Neurol., Brain Res., Exp. Brain Res., Science, Grant Proposals for National Science Foundation and NIH.
Site Visitor at Irvine Medical Center for Extramural Research Branch NIAAA
Reviewer, National Institute of Mental Health, Basic Psychopharmacology and Neuropsychology Research Review

Recent Publications

Brons, J.F. and Woody, C.D. Long-term changes in excitability of cortical neurons after Pavlovian conditioning and extinction. J. Neurophysiol. 44:605-615, 1980.

Sakai, H. and Woody, C.D. Identification of auditory responsive cells in the coronal-pericruciate cortex of awake cats. J. Neurophysiol. 44:223-231, 1980.

Brons, J.F., Woody, C.D., and Allon, N. Changes in the excitability to weak intensity electrical stimulation of units of the pericruciate cortex in cats. J. Neurophysiol. 47:377-388, 1982.

Woody, C.D. Memory, Learning, and Higher Function: A Cellular View. Springer-Verlag, New York, 1982, pp. 1-483.

Kim, E.H.-J., Woody, C.D., and Berthier, N.E. Rapid acquisition of conditioned eye blink responses in cats following pairing of an auditory CS with glabella tap US and hypothalamic stimulation. J. Neurophysiol. 49:767-779, 1983.

Woody, C.D., Kim, E.H.-J., and Berthier, N.E. Effects of hypothalamic stimulation on unit responses recorded from neurons of sensorimotor cortex of awake cats during conditioning. J. Neurophysiol. 49:780-791, 1983.

Allon, N., and Woody, C.D. Epileptiform activity induced in single cells of the sensorimotor cortex of the cat by intracellularly applied scorpion venom. Exper. Neurol. 80:491-497, 1983.

Woody, C.D. The electrical excitability of nerve cells as an index of learned behavior. In: Princeton Symposium on "Primary Neural Substrates of Learning and Behavioral Change". D. Alkon and J. Farley, (Eds.). Cambridge University Press, Cambridge, 1984, pp. 101-127.

Berthier, N.E., and Woody, C.D. An essay on latent learning. In: The Neuropsychology of Memory. N. Butters and L.R. Squire (Eds.). Guilford Press, New York, 1984, pp. 504-512.

Woody, C.D. Studies of Pavlovian eyeblink conditioning in awake cats. In: Proceedings of the Conference on the Neurobiology of Learning and Memory. G. Lynch, J. McGaugh, and N. Weinberger (Eds.). Guilford Press, New York, 1984, pp. 181-196.

Woody C.D., Gruen, E., and McCarley, K. Intradendritic recordings from neurons of motor cortex of cats. J. Neurophysiol. 51:925-938, 1984.

Woody, C.D., Alkon, D.L., and Hay, B. Depolarization-induced effects of intracellularly applied calcium-calmodulin dependent protein kinase in neurons of the motor cortex of cats. Brain Res. 321:192-197, 1984.

Aou, S., Woody, C.D., Oomura, Y., Nishino, H., and Lenard, L. Effect of hypothalamic stimulation on intracellular neuron activity of motor cortex in awake monkeys. Neurosci. Letter Suppl., 17:s60, 1984.

Swartz, B.E., and Woody, C.D. Effects of intracellular antibodies to cGMP on responses of cortical neurons of awake cats to extracellular application of muscarinic agonists. Exp. Neurol. 86:388-404, 1984.

Woody, C.D., Bindman, L.J., Gruen, E., and Betts, B. Two different mechanisms control inhibition of spike discharge in neurons of cat motor cortex after stimulation of the pyramidal tract. Brain Res. 332:369-375, 1985.

CURRICULUM VITA

Name: Nahum Allon

PII Redacted [redacted]

Present Address: Israel Institute of Biological Research
Ness Ziona 70450 ISRAEL

1963-1966: Military Service as an officer

1967-1970: B.Sc. in Biology, Tel Aviv University

1970-1973 "Studies on venom synthesis, secretion and injection in viperid snakes" M.Sc. thesis under the supervision of Prof. E. Kochva, in the Department of Zoology, Tel Aviv University

1974-1979: "Neural activity in the medial geniculate body of squirrel monkey (Saimiri sciureus) in response to auditory stimuli" Ph.D. thesis under the supervision of Dr. Z. Wollberg in the Department of Zoology, Tel Aviv University

1979-1982 Assistant Research Psychophysiologist
Neuropsychiatric Institute, UCLA
Supervisor: C.D. Woody, M.D.

1983- Israel Institute of Biological Research

Recent Research:

1. Changes in excitability of units in cat pericruciate cortex to weak extracellular stimulation during conditioning

2. The ionic mechanism underlying the excitation of cells in the motor cortex by weak extracellular currents

PUBLICATIONS:

Allon, N. and Kochva, E. (1972) Amount of venom injected into mice and rats by Vipera palaestina in a single bite. Am. Zool. 12:685.

Kochva, E., Oron, U., Bdolah, A., and Allon, N. (1972) Regulacao da secrecao e injecao de venamo em sepentes viperideos. Simposio: "Aplicacao de venenos das serpentes em Problemas de Farmacologia e Bioquimica cellular". Ribeirao Preto S.P. Brazil.

Allon, N. and Kochva, E. (1974) The quantities of venom injected into prey of different sizes by Vipera palaestina in a single bite. J. Exp. Zool. 188:71-76.

Kochva, E., Oron, U., Bdolah, A., and Allon, N. (1975) Regulation of venom secretion and injection in viperid snakes. Toxikon 13:104.

Allon, N. and Wollberg, Z. (1978a) Superior colliculus of squirrel monkey: Responses of single cells to auditory stimuli. Abstract presented in the Israel Society of Physiology and Pharmacology.

Allon, N. and Wollberg, Z. (1978b) Responses of cells in the medial geniculate body (MGB) of squirrel monkey to auditory stimuli. Neurosci. Ltrs. Suppl. 1:52.

Allon, N. and Wollberg, Z. (1980) The response properties of cells in the medial geniculate body (MGB) of awake squirrel monkey to species specific vocalization. Soc. Neurosci. Abstr. 6:333.

Allon, N., Yeshurun, Y., and Wollberg, Z. (1981) Responses of single cells in the medial geniculate body of awake squirrel monkey. Exp. Brain Res. 41:222-232.

Yeshurun, Y., Allon, N., and Wollberg, Z. (1981) A computer aided simulation of an electrode penetration into deep brain structures. Computers and Biomed. Res. 14:19-31.

Brons, J.F., Woody, C.D., and Allon, N. (1982) Changes in the excitability to weak intensity extracellular electrical stimulation of units of the pericruciate cortex in cats. J. Neurophysiol. 47:377-388.

Allon, N., and Woody, C.D. (1982) Initiation of paraoxysmal depolarization shifts in single cells of the sensorimotor cortex of awake cats by scorpion venom (Centruroides sculpturatus). Soc. Neurosci. Abstr. 8:101.

Allon, N., and Woody, C.D. Epileptiform activity induced in single cells of the sensorimotor cortex of the cat by intracellularly applied scorpion venom (Centruroides sculpturatus). Exp. Neurol., 1983, in press.

CURRICULUM VITAE

Name: Shuji Aou

PII Redacted [redacted]

[redacted]

Present Address: Department of Biological Control System, National Institute, Physiological Sciences, Myokaiji, Okazaki 444, JAPAN

Education:

1977 - M.D. (Medical B.S.)
Faculty of Medicine, Kyushu University

1982 - Ph.D. (Doctor of Medical Science)
Faculty of Medicine, Kyushu University

Positions Held:

1982- Research associate, Department of Biological control system, National Institute for Physiological Sciences, Okazaki

1983- Instructor (part-time), Department of Physiology, Nihon University School of Medicine, Itabashi, Tokyo

1984- Instructor (part-time), Department of Physiology, Faculty of Medicine, Kyushu University, Fukuoka

Professional Societies:

Member, Japan Physiological Society
Member, Society of Psychosomatic Medicine, Japan

Recent Publications

Aou, S., Oomura, Y., Nishino, H., Ono, T., Yamabe, K., Sikdar, S.K., and Noda, T. Functional heterogeneity of single neuronal activity in the monkey dorsolateral prefrontal cortex. Brain Res. 260:121-124, 1983.

Aou, S., Oomura, Y., Nishino, H., Inokuchi, A., and Mizuno, Y. Influence of catecholamines on reward-related neuronal activity in monkey orbitofrontal cortex. Brain Rex. 267:165-170, 1983.

Aou, S., Oomura, Y., and Nishino, H. Influence of acetycholine on neuronal activity in monkey orbitofrontal cortex during bar press feeding task. Brain Res. 275:178-182, 1983.

Inoue, M., Oomura, Y., Nishino, H., Aou, S., Sikdar, S.K., Hynes, M., Mizuno, Y., and Katafuchi, T. Cholinergic role in monkey dorsolateral prefrontal cortex during bar press feeding task. Brain Res. 278:185-194, 1983.

Hori, T., Kiyohara, T., Oomura, Y., Nishino, H., and Aou, S. Unit activity in the monkey orbitofrontal cortex during thermoregulatory and feeding behaviors. J. Physiol. Japan 45:594, 1983.

Aou, S., Oomura, Y., Lenard, L., Nishino, H., Minami, T., Misaki, H., and Inokuchi, A. Behavioral significance of monkey hypothalamic glucose-sensitive neurons. Brain Res., in press.

Aou, S., Woody, C.D., Oomura, Y., Nishino, H., and Lenard, L. Effect of hypothalamic stimulation on intracellular neuron activity of motor cortex in awake monkeys. Neurosci. Letter Suppl. 17:s60, 1984.

Aou, S., Woody, C.D., Oomura Y., and Nishino, H. Effects of reward-related hypothalamic stimulation on neuron activity of the motor cortex in the monkey. Soc. Neurosci. Abstr. 10:312, 1984.

Curriculum vitae, Tamas Bartfai

PII Redacted

[redacted]

1966-1971	Graduate studies at Eötvös Loránd University, Faculty of Natural Sciences, in Chemistry, physics and mathematics
1971-1973	Graduate studies in biochemistry at the Department of Biochemistry, University of Stockholm.
1973	Ph.D. in biochemistry: (Thesis: Mathematical modeling in enzyme kinetics; Steady state kinetic model of glyoxalase I).
1973-	Teaching at the Department of Biochemistry, University of Stockholm.
1975	Docent in Biochemistry

Professional experience

1963-1970	Research associate at the Central Research Institute for Physics, Budapest.
1970	Mathematical modeling for the Bureau of Chemical Engineering, Budapest.
1972-1973	Instructor in Biochemistry, Stockholm.
1973	Lecturer in Biochemistry. (Teaching on graduate courses General Biochemistry, Enzymology, Neurochemistry).
1974 (June, August)	Visiting scientist at Hadassah Medical School, Jerusalem, in Professor Shimon Gatt's laboratory.
1976 Jan-1977 June	Visiting Assitant Professor at Yale University, Medical School, Department of Pharmacology in Professor Paul Greengarrd's laboratory: Research and teaching.
1977 July	Appointed as senior lecturer or "tenured Assoc. Professor" in the Department of Biochemistry, Arrhenius Laboratory, University of Stockholm. Chairman Professor Lars Ernster.

Invited symposia lecture were given:

Linderström-Lang Conference 1974, Oslo, organizer Dr. E. Kvamme.

Cholinergic Meeting 1977, La Jolla, organizer Dr. D.J. Jenden.

International Congress of Neurochemistry, Copenhagen, 1977.

Cyclic Nucleotides and CNS, Treverro, Italy, 1977.

International symposium on Cholinergic Mechanisms 1980, Florence, Italy.

Meeting of European Society for Neurochemistry, Catania, 1981.

Symposium on Peptides in the CNS, Weizmann Institute, 1981.

Symposium on Cholinergic Mechanisms at the Council of Europe, Strassbourg, 1982.

European Symposium on Cell Regulation, Strassbourg, 1983.

Meeting of the International Society for Neurochemistry, Vancouver, 1983.

"On Neural Substrates of Conditioning", Symposium in Woods Hole, 1983.

Seminars:

Hadassah, Dept. of Biochemistry, Jerusalem.
Weizmann Institute, Rehovot
Yale University, Dept. of Pharmacology
Harvard University, Dept. of Neurobiology
Columbia University, Section of Neurobiology
UCLA, Dept. of Pharmacology
Ciyt of Hope
Tel Aviv University, Dept. of Biochemistry
NIH, Preclinical Pharmacology
Rockefeller University
University of Maryland
Marine Biological Station, Woods Hole
Mario Negri Institute, Milan

Served as a teacher on the courses in Neurochemistry organized by the European Molecular Biology Organization.

Awards:

1966	Eötvös Prize in Chemistry
1976	European Molecular Biology organisation long term fellowship
1977	Liljevalch's Jr. Stipend
1978	Ekströms Stipendium
1982/83	Fellowship from the University of Stockholm for research for senior lecturers.

Research support:

Swedish Medical Research Council
Swedish Cancer Society
National Institute of Mental Health, Bethesda
Swedish Board for Planning Research

Letters of recommendation could be obtained from Professor Lars Ernster, Department of Biochemistry, Arrhenius Laboratory, 106 91 Stockholm, Sweden. Professor Paul Greengard, Department of Pharmacology, Yale University Medical School, Cedar str 333, New Haven, Conn 06510, USA. Professor Shimon Gatt, Department of Biochemistry, Laboratory of Neurochemistry, Hadassah Medical School, Hebrew University, Jerusalem POB 1172, Israel.

RECENT PUBLICATIONS

1. Bartfai, T., Nordstrom, O., and Tjornhammar, M.L. Cyclic guanosine 3'5'-monophosphate in the nervous system. Pre-, post- and transsynaptic effects. Progress in Pharmacol. 4/1, 151-157, (1980).

2. Lundberg, J.M., Hedlund, B., and Bartfai, R. Vasoactive intestinal polypeptide (VIP) enhances muscarinic ligand binding in the cat submandibular salivary gland. Nature 5845, 147-149, (1982).

3. Hedlund, B., Grynfarb, M., and Bartfai, T. Two ligands may bind simultaneously to the muscarinic receptor. Naunyn-Schiedeberg's Arch. Pharmacol. 320, 3-13 (1982).

4. Alberts, P., Bartfai, T., and Stjarne, L. Atropine effects on ^{3}H-acetylcholine secretion from guinea pig myenteric plexus evoked electrically or by high potassium. J. Physiol. 329, 93-112 (1982).

5. Hedlund, B., Abens, J., and Bartfai, T. Chronic atropine treatment induces supersensitivity of VIP receptors and muscarinic receptors in the rat salivary gland, Science 200, 519-520, (1983).

6. Tjornhammar, M.L., Lazaridis, G., and Bartfai, T. Cyclic GMP efflux from liver slices, J. Biol. Chem. 258, 6882-6886, (1983).

7. Lundberg, J.M., Hedlund, B., Anggard, A., Fahrenkrug, J., Hokfeldt, T., Tatemoto, K., and Bartfai, T. Costerage of peptides and classical transmitters in neurons. Media Hoecht Bd. 18, 8, 1-9, (1983).

8. Peterson, L.L., and Bartfai, T. In vitro and in vivo inhibition of ^{3}H-imipramine binding by cadmium. Eur. J. Pharm. 90, 289-292, (1983).

Curriculum Vita

Neil E. Berthier

April 1983

PII Redacted I. [redacted]

II. Educational Background:

A. Attended University of Massachusetts, Amherst, Ma. from September 1975 to November 1980. M.S. May, 1978, Ph.D. February, 1981. Psychology, concentration in Neurobiology of Learning and Memory, Advisor J.W. Moore.

B. Attended Virginia Polytechnic Institute and State University, Blacksburg, Va. from September 1971 to March, 1975. B.S. June 1975 with Distinction in Psychology.

C. Graduate Courses Taken:

Statistical Inference in Psychology
Physiological Psychology
Neuroanatomy
Advanced Applied Statistics
Conditioning
Comparative Neurophysiology
Psychopharmacology
Animal Learning
Human Information Processing
Neurobiology of Learning and Memory
Developmental Neurobiology
Experimental Neurophysiology

Courses Audited:

Calculus I, II, and Multivariate Calculus
Minicomputers
Neurochemistry

D. Student in the January 1982 Neurobiology course at the Marine Biological Laboratory, Woods Hole, Ma.

III. Professional Positions:

A. Assistant Research Neurobiologist, January, 1981 to present, Department of Psychiatry, Mental Retardation Research Center, Neuropsychiatric Institute, UCLA Medical Center, Los Angeles, Ca

B. Teaching Assistant and Associate, September 1975 to May 1980, University of Massachusetts, Amherst Ma. Assisted and prepared exams and lectures for courses in Physiological Psychology, Animal Learning, Statistics, Methods, and Introductory Psychology.

IV. Professional Specialties and memberships:

Neurobiology of Learning and Memory, Animal Learning.

Member of the Society for Neuroscience

V. References:

Dr. J.W. Moore, Department of Psychology,
University of Massachusetts, Amherst Ma. 01003

Dr. C.D. Woody, Departments of Psychiatry and Anatomy
University of California Los Angeles, Los Angeles, Ca. 90024

Dr. D.L. Alkon, Laboratory of Biophysics, Marine Biological Laboratory, Woods Hole, Ma. 02543

Dr. G.A. Wyse, Department of Zoology,
University of Massachusetts, Amherst Ma. 01003

VI. Publications and Presentations:

Berthier, N.E., Spinelli, D.N., Solomon, P.R. & Moore, J.W. Fiber-sparing lesions of the central nervous system produced by cyanide. Presented by Moore at the European Brain and Behavior Society's workshop on the Cerebral Commissures. Rotterdam, March, 1977.

Moore, J.W., Yeo, C. & Berthier, N.E. Brain mechanisms of Pavlovian inhibition. Presented at the Annual meeting of the Psychonomic Society, San Antonio, 1978.

Powell, G.M., Berthier, N.E. & Moore, J.W. Efferent neuronal control of the nictitating membrane in rabbit (Oryctolagus cuniculus): A reexamination. Physiology & Behavior, 1979, 23, 299-308.

Berthier, N.E. & Moore, J.W. Role of the extraocular muscle in rabbit (Oryctolagus cuniculus) nictitating membrane response. Physiology & Behavior, 1980, 24, 931-937.

Berthier, N.E. & Moore, J.W. Spatial differential conditioning of the nictitating membrane response in hippocampectomized rabbits. Physiological Psychology, 1980, 8, 451-454.

Berthier, N.E. & Moore, J.W. Disrupted conditioned inhibition of the rabbit nictitating membrane response following mesencephalic lesions. Physiology & Behavior, 1980, 25, 667-673.

Berthier, N.E. & Moore, J.W. Multiple unit activity of the abducens nerve in the anesthetized and paralyzed rabbit. Society for Neuroscience Abstracts, 1980, 6, 427.

Berthier, N.E., Betts, B. & Woody, C.D. Rapid eyeblink conditioning: response topography. Society for Neuroscience Abstracts, 1981, 7, 750.

Desmond, J.E., Berthier, N.E. & Moore, J.W. Brains stem elements essential for the classically conditioned nictitating membrane response of rabbit. Society for Neuroscience Abstracts, 1981, 7, 650.

Moore, J.W., Berthier, N.E. & Desmond, J.E. Brain stem electrophysiological correlates of the classically conditioned nictitating membrane response in rabbit. Society for Neuroscience Abstracts, 1981, 7, 358.

Moore, J.W., Desmond, J.E. & Berthier, N.E. The metencephalic basis of the conditioned nictitating membrane response. In Conditioning: Representation of Involved Neural Functions. C.D. Woody (Ed.), New York: Plenum, 1982.

Berthier, N.E., Betts, B. & Woody, C.D. Discrimination conditioning of eyeblink with aversive brain stimulation. Society for Neuroscience Abstracts, 1982, 8, 315.

Berthier, N.E. & Moore, J.W. The unconditioned nictitating membrane response: The role of the abducens nerve and nucleus and the accessory abducens nucleus in the rabbit, Brain Research, 1983, 258, 201-210.

Kim, E.H-J., Woody, C.D. & Berthier, N.E. Rapid acquisition of conditioned eyeblink responses in cats following pairing of an auditory conditioned stimulus with glabella tap unconditioned stimulus and hypothalamic stimulation, Journal of Neurophysiology, 1982, 49, 767-779.

Woody, C.D., Kim, E.H-J. & Berthier, N.E. Effects of hypothalamic stimulation on unit responses recorded from neurons of the sensorimotor cortex of awake cats during conditioning, Journal of Neurophysiology, 1982, 49, 780-791.

CURRICULUM VITAE

Name: Dr. Lynn J. Bindman [redacted]

Address: Department of Physiology
University College London
PII Redacted Gower Street, LONDON WC1E 6BT

[redacted]

Education: South Hampstead High School for Girls, London
University College London, Department of Physiology
1957-1963

Degrees: BSc London 1960 Class Upper II
PhD London 1964 Physiology of the cerebral cortex

Posts held: Honorary Research Assistant, Department of Physiology, UCL, Grant awarded by Medical Research Council 1963-1965

Assistant Lecturer (part-time) Department of Physiology, UCL 1965-1969

Research Associate (part-time) Department of Physiology, UCL. Grant awarded by Medical Research Council 1969-1972

Lecturer, Department of Physiology, UCL 1972-

Membership of Societies

The Physiological Society - elected 1967
Education sub-committee - appointed 1981
The Pharmacological Society - elected 1976
International Brain Research Organisation - elected 1978
Brain Research Association

Research:

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CURRICULUM VITA

Name: Dorwin Birt

[redacted] PII Redacted

Education:

B.S., Purdue University, June 1968. Major: Psychology; minors Chemistry and Mathematics

Ph.D., Indiana University, October 1974 - Physiological Psychology.

Professional Experience:

Assistant Research Psychologist, Neuropsychiatric Institute, UCLA
August 1982 to present

Neurophysiologist, Huntington Medical Research Institutes
January 1982 to present

Visiting Research Associate, California Institute of Technology
January 1982 to present

Senior Research Fellow, Division of Biology, California Institute of Technology
1977 to 1982

Research Fellow, Division of Biology, California Institute of Technology
1974 to 1977

Research Associate, Center for Neuroscience, Indiana University
1973-74

Publications

Stewart, D. L., Birt, D. L. and Towns, L. C. Visual receptive field characteristics of superior colliculus neurons after cortical lesions in the rabbit. Vision Res. 13: 1965-1977 (1973).

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Name: Haing-Ja Kim

PII Redacted

[redacted]

[redacted]

Sex: Female

Education:

B. S., 1967: Major; Physics: Minor; Mathematics: 1962-1967, Seoul National University, Korea
1971-1972, Special student at Korea University, Korea
Major fields: Psychology and Biology
1973 (Jan.-June), Special student at Western College, Ohio,
Major fields: Psychology and Biology
1973 (Sept.-Dec.), Graduate study at Bucknell University, Pennsylvania,
Major field: Physiological Psychology
M. A., 1976: Major; Psychology: 1974-1976, Northwestern University
Major field; Neuroscience and behavior
Ph. D., 1978: Major; Psychology: 1976-1978, Northwestern University, Evanston, Illinois
Major field; Neuroscience and behavior

Dissertation topic: Histochemical fluorescence study of the substantia nigra and role of the nigroneostriatal dopaminergic system in memory and motor functions.

Special Awards:

1973: University Scholarship, Western College & Bucknell Univ.
1974-1975: University Fellowship, Northwestern University
1975-1976: Teaching Assistantship, Northwestern University
1976-1977: University Fellowship, Northwestern University
1977-1978: Research Assistantship, Northwestern University
1974-1977, Summer: Research Assistantship and Walter-Dill-Scott Fellowship, Northwestern University

Professional Experience:

1969-1971: Teaching assistant in Introductory Physics, Seoul National University, Korea
1975-1976: Teaching assistant in Introductory Psychology and Elementary Statistics, Northwestern University
1978, August-present: Post-doctoral research; Intracellular recording from cortical motor neurons in cats

Name: Haing-Ja Kim

References:

1) Aryeh Routtenberg, Professor of Psychology and Biological Sciences, Cresap Neuroscience Laboratory, Northwestern University

2) J. Peter Rosenfeld, Professor of Psychology, Cresap Neuroscience Laboratory, Northwestern University

3) Ronald Clavier, Professor of Anatomy, School of Medicine, Northwestern University

4) Rebecca M. Santos, Research Associate, Department of Opthalmology, Medical Center, University of Illinois, Chicago Campus

Publications:

1) Kim, H.-J. and Routtenberg, A. Retention disruption following post-trial picrotoxin injection into the substantia nigra. Brain Research, 1976, 113, 620-625.

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1) Kim, H.-J. and Routtenberg, A. The cytoarchitecture of the rat substantia nigra: Catecholamine fluorescence and Nissl-staining of identical Vibratome sections.

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CURRICULUM VITAE

Name: Michikazu Matsumura

PII Redacted [redacted]

Present Address: Kyoto University
Primate Research Institute
Inuyama City, Aichi 484 JAPAN

Education

1969.4	Department of Biophysics	Major: Molecular Physiology
- 1973.3	Kyoto University	Degree: B. A.
1973.4	Primate Res. Inst.	Neurophysiology
- 1975.3	Kyoto University	Degree: Master
1975.4	Primate Res. Inst.	Neurophysiology
- 1978.3	Kyoto University	Degree: Ph. D.

Scholarship and Relevant Employment

1973 - 1974 Scholarship from Japanese Government
Location: Primate Res. Inst., Kyoto University
Supervisor: K. Kubota, M.D.
Responsibilities: Unit and field potential recording from monkey prefrontal cortex in awake and in anesthetized state.

1975 Inter-University Exchange Program
Location: Dept. Biological Engineering, Osaka University
Supervisor: N. Tsukahara, M.D.
Responsibilities: Intracellular studies in cat red nucleus and reticular formation after an ablation of cerebellar nuclei.

1976 - 1977 Scholarship from Japanese Government
Location: Primate Res. Inst., Kyoto University
Supervisor: K. Kubota,
Responsibilities: Intracellular recording from monkey motor cortex during voluntary movement.
(Doctoral Thesis)

1978 Post-Doctoral Fellow
Location: Primate Res. Inst., Kyoto University
Supervisor: K. Kubota
Responsibilities: Histological studies of cortico-cortical afferents to hand area of monkey motor cortex with horseradish peroxidase.

1978 - present
Assistant Research Neurobiologist
Location: Neuropsychiatric Inst., UCLA
Supervisor: C.D. Woody, M.D.
Responsibilities: Intracellular investigation of excitability changes in facial motoneurones in conditioned cat.

Publications (papers)

Matsumura, M.
Intracellular synaptic potentials of primate motor cortex neurons during voluntary movement.
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VI. APPENDIX

Excerpted from : Memory, Learning, and Higher Function by Charles D. Woody
Springer-Verlag, New York, 1982.

Chapter 7

Cybernetics: A Means for Analysis of Neural Networks

The development of the statistical theory of communication is a landmark in the history of communication theory. Our primary concern in a communication or control problem is the flow of messages. Since the central idea in the statistical theory is that messages and noise should be considered as random phenomena, the theory incorporates probability theory and generalized harmonic analysis in its foundation.

(Y. W. Lee, 1960)

Commonsense approaches to an understanding of "higher function" are useful but, as we have seen, are basically introspective. Such approaches could be ill advised if used analytically because of their intrinsic susceptibility to errors, particularly those of the type illustrated in Fig. 6.6. Other, more objective means must be found to analyze the complex integrative functions of neural networks. As our knowledge of anatomically and physiologically based memory and learning advances, so must our expression of this knowledge. The form of this improved expression is likely to be mathematical and as specific as expression of our modern knowledge of genetics and the genetic codes. The purpose of this chapter is to explore some of the forms that are likely to serve for expression of our knowledge of memory and learning.

Analysis of large populations of neurons can, in principle, be approached from the same standpoint as analysis of numerically small reflex networks. The analysis requires application of systems approaches from engineering disciplines plus consideration of the limiting physiologic constraints that apply to each system analyzed. In addition, since large populations of neurons deal substantially with the processing of information, their overall analysis requires concepts from information theory.

This concluding chapter examines possible means for analyzing complex systems using mathematics, engineering, and physics. The approach is called systems analysis, but when applied to adaptive systems, it is more properly

termed cybernetics, the analytic science that deals with the control of information processing in man and machine. By using the techniques described herein, a rigorous analysis can be made of *linear* information processing systems and, perhaps, of some nonlinear systems as well [582,583,1086]. Some reflexes within the brain can be assumed to behave as a linear system and can be investigated by linear systems analysis [429,1123]. Such an analysis, though properly applicable only to theoretical systems meeting strict statistical criteria, still provides the most useful beginning toward a rigorous analysis of complex nerve networks. It simplifies the complexities of the networks, leads to formulations of the transforms of given inputs into particular outputs, and generates more precise transforms than those presently existing.

A few suitable *models* of information transfer in the brain have been developed that are amenable to mathematical analysis [cf. 18-22,366,838-841, 883,1033-1038]. The most elegant of these deals with image recognition, i.e. the transmission and processing of sensory labeled messages arising at the receptors. Minsky and Papert [672] have transformed certain problems of image recognition into problems of geometry—a transformation that elegantly simplifies many problems of analysis. Then, they have devised a theorem, the Group Invariance Theorem, that provides a general analytic solution for one set of the geometry. In application, the Group Invariance Theorem (p. 388) adequately describes the geometry of sensory reception for the components of two specific models of elements of an image recognition network, the perceptron and the informon. In these models, as in the brain itself, line labeling appears to be the key to following the flow of information through its complex transformation from sensory input into motor output. Flowgraphs and linear systems analysis are also helpful in this regard.

Each of these analytic approaches properly begins by considering known constraints on the system to be analyzed. Therefore, before discussing the models and their analysis, some constraints on information processing that any useful model of brain function should satisfy will be considered.

Constraints

Time Constants of Neural Information Flow

How rapidly can information be transmitted and processed within the CNS?

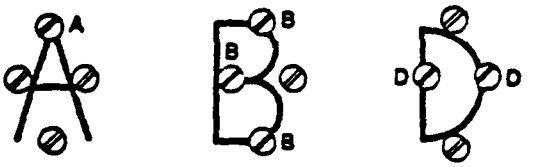
Conduction Time and Transmission Delay

As noted earlier in Chapter 2, the rate of nerve conduction is a function of fiber size, with large axons conducting more rapidly than small axons. Transmission of an electrically propagated impulse along a neuron may proceed as rapidly as 160 m/sec in the dorsal spinocerebellar tract of the cat [369] or as slowly as 0.5 m/sec in the finest, unmyelinated axons of the spinothalamic system [693]. Thus, while it could take as little as 2 msec for proprioceptive information concerning hindleg position to reach the cerebellum of the cat (a distance of about 320 mm), it could take as long as 640 msec for infor-

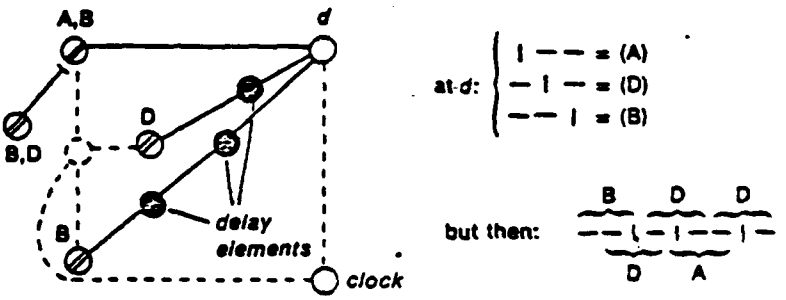
* * * * * * * * * * *

Automata Design

I. Receptors



II. Spatial signal-serial processor-temporal code



III. Spatial signal-parallel processor-Spatial code

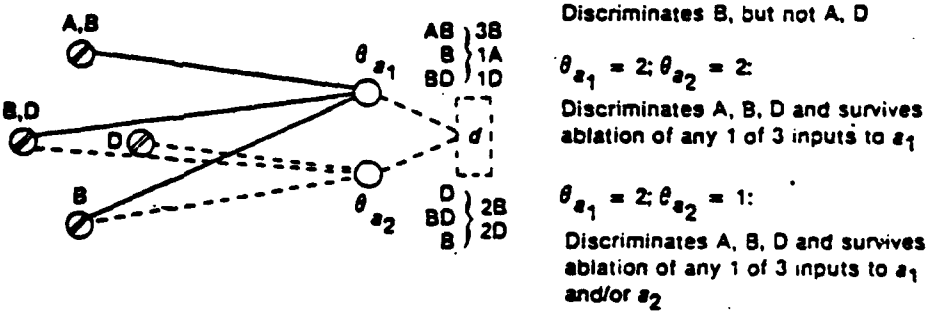
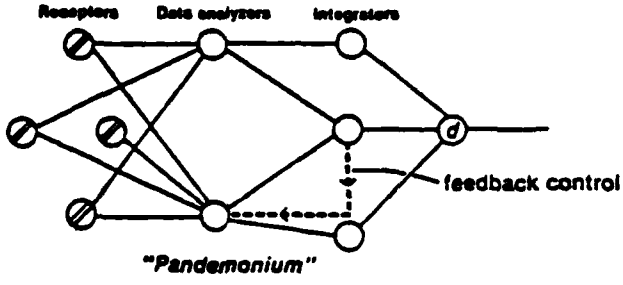


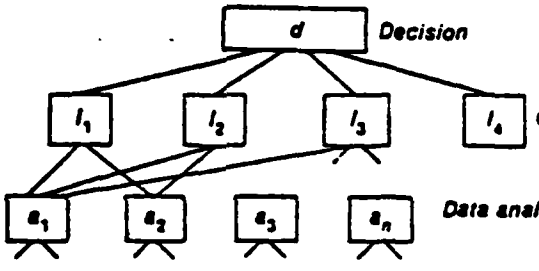
Fig. 7.5. Examples of the components of different automata. I. Receptor elements common to each example. The uppermost of the four elements is receptive to (and intersected by) the letters A and B but not D. The lowest element is receptive to B only. The receptivity of the remaining two elements is as indicated. II-IV. Automata with different network architectures: II, serial time dependent, III, parallel perceptron, IV, parallel pandemonium. In II three

IV. Feature weighting and analysis plus feedback control



"Pandemonium"

V. Feature detection and evolution



a_1, a_2, a_3,... are various analytic operators: e.g., template matching, summing, differentiating, etc.

Selection is based on the sum W_i of the weightings λ_i of the a_j individual features analyzed

different coded outputs of the decisional element, d, are shown to the right. Below, the ambiguity of this coding is illustrated when its beginning in time is uncertain. In III changing θ, the number of inputs required to fire the second order elements, changes the discriminative property of the network as discussed in the text and summarized in the diagram to the right. In IV a variation on III introduces feature detection (e.g., summation, filtering, etc.) as well as feedback control (heavy dashed line) into the circuit. A version of IV is shown below (V) in which details have been inserted after Selfridge's pandemonium [883]. Selection of evaluation of the individual demons for permutation is based on W_i, the sum of the weightings, λ_i, of the individual feature detectors, a_j.

The filled circles represent serial time delay elements. The elements comprised by dashed lines represent a clocking mechanism that keeps track of time following presentation of the stimulus pattern at the receptors. Depending on which receptor is activated, a time coded signal 1--, -1-, or --1 will be generated at the decision-making element, d. Note that if track

is not kept of time (see Fig. 7.5, II, lower right), the code becomes ambiguous. Though the example is oversimplified, it is quite representative of the type of processing that is widely used in digital computers.

The term parallel processing was originally used to designate performance of the same processing operation by more than one channel at a time. The purpose was to support majority logic and redundant signal processing as discussed earlier. *Multiplexed*, parallel processing resembles much of the processing done by the brain. In the example shown in Fig. 7.5, III, the second-order elements receive redundant messages and parallel processing is used to generate a "decisional" output at element "d". As can be seen, this type of processing has remarkable sorting or discriminative properties when adaptation is introduced.

If each of the second order elements in Fig. 7.5 III is set to fire when three inputs are received (3/3), the network will distinguish B, but not A from D, i.e., a_1 (fires) = B. If the "threshold" is reduced to discharge upon reception of two inputs (2/2), the network will then discriminate A, B, and D. An A will be designated by no discharge, a B by discharge of both elements, and a D by discharge of the lower element, i.e., $\overline{a}_1\overline{a}_2$ = A (or nothing presented), a_1a_2 = B, $\overline{a}_1a_2$ = D. Moreover, the network will continue to function despite destruction of any one of the three input lines to the upper element.

Although one must beware of making exact transpositions between mechanical and physiologic models, many of the same, general theoretical considerations concerning learning, memory, and even higher function apply to machines as to physiologic systems. The machines give us a physical model which is more accessible to analysis and is more easily studied. Three machine automata stand out from the others in providing insightful models of learning operations, component interactions, and the constraints thereof. They are the perceptron, pandemonium, and the informon.

Perceptron

The perceptron represents an early attempt by Rosenblatt and colleagues to develop a learning automaton based on their conceptions of brain organization [838-841]. In this device, the components consist simply of modifiable elements and their interconnections. As shown in Fig. 7.26, α is the sum of the components $\varphi_{(\chi)}$, each weighted by α_φ. When the weightings are modified ($\Delta\alpha$), the system can adapt to distinguish a particular input, identified when ψ is $\geq$ some predetermined value, θ.

$$\psi = \Sigma \alpha_\varphi \varphi(\chi) \geq \theta], \tag{7.2}$$

where $\Delta\alpha$ reflects adaptation.

The example of parallel processing (Fig. 7.5, III) can be viewed as a perceptron by making d = Σ and considering a_1 and a_2 as having weighted inputs depending on the threshold settings, θ_a.

In such systems, the performance of pattern recognition can be adaptively improved with relatively simple algorithms of element modification as illustrated in Fig. 7.5 (additional algorithms are listed on p. 395). Although this can be done among elements with randomly organized connections, as the original perceptron demonstrated, a more efficient operation will be provided by a nonrandomly organized network. Thus, the organization of the adaptive network may become a critical variable in the learning operations that are performed by such a system.

Pandemonium

An example of a nonrandomly organized automaton is *pandemonium* of Oliver Selfridge [883]. Its organization is hierarchical, being characterized by multiple layers supporting different operations as shown in Fig. 7.5, IV and V. The initial layer again consists of simple receptor or data collecting elements, termed data demons by Selfridge. The second layer consists of specialized analyzers or computational demons. They process incoming data by stereotyped procedures such as matched filtering, summation, or differentiation. The third layer consists of integrators or cognitive demons. They integrate weighted inputs from various computational demons. Finally, a decision maker or "decision demon" selects the loudest or most active cognitive demon(s) and by its (their) identity gives priority to a selected set of receptors.

Within this hierarchy, adaptation occurs according to rules of reinforcement specified in terms of the effectiveness of each element in performing the selected recognition task. Elements which are more contributory to successful image recognition are positively reinforced by increasing their weighting. Elements which are less contributory are eliminated. Permutations of the analytic algorithms of successful elements are generated to replace those of unsuccessful elements. Hill-climbing techniques are used to secure continued improvements of the adaptations with extensive attention paid to the problem of avoiding false peaks.

Several insights into adaptive information processing are provided by pandemonium. Pandemonium is characterized as a chaotic operation with demons, subdemons, and sub-subdemons shrieking their outputs, adapting, deciding, and sometimes evolving. However, the chaos turns out to be more orderly than expected. All the analytic functions are particularized and are, to a significant degree, predetermined. Despite the great degree of adaptability within the hierarchy, the hierarchy is relatively fixed. The reason for this is that, although the adaptability permits evolution, it is along a predictable pathway, and occurs within a particular hierarchy. (This feature appears to have led this particular automata to a particularly tenacious pursuit of false peaks during hill-climbing adaptive operations.) Differences in the design of the hierarchy selected for Pandemonium versus that shown in Fig. 3.42 may therefore be of some consequence. The ability to switch between elements may need to be matched by an ability to switch between hierarchies.

Informon

The *informon* model of Uttley [1033-1038] takes a somewhat different approach to the design of an automaton, concentrating on improving the construction of the fundamental adaptive element itself. The basic informon consists of a single element with multiple inputs $F(x_n)$ and an output (Fig. 7.6). The inputs have variable weightings, α. One of the inputs is defined as a reinforcing input $F(z)$ with a fixed negative weighting, $-k$. There is also provision for negative feedback of information concerning the operational state of the element, $F(Y)$. The negative feedback is required for stability of the adaptive process. $F(Y)$ is some function of the output of the element prior to the state of binary, spike discharge. There is finally a threshold device, θ, at or just before the output, which can be used to discriminate between different sets of inputs.

Several additional variables (or constraints) are required for the informon to discriminate successfully one particular input $F(x_i)$ from another, $F(x_{ii})$. These are:

1. The algorithm by which α_i is altered ($\Delta\alpha$).
2. The need for a reinforcing input, $F(z)$, to distinguish or identify which input signal is the particular signal to be discriminated.
3. The need to achieve some system normalization through negative (not positive) feedback of information regarding the current system state, $F(Y)$.

Note also that by picking the adaptive algorithm correctly (e.g., log of the mutual information between inputs), one can greatly facilitate both normalization and input discrimination.

Algorithm for $\Delta\alpha$

The trick here is to choose an algorithm that will produce S-shaped adaptive operations such as are found with conditioning or other simple forms of learning. It will also be useful to have a decay or extinction phase of adaptation. Adaptation is performed by changing the weighting, α, of an input.

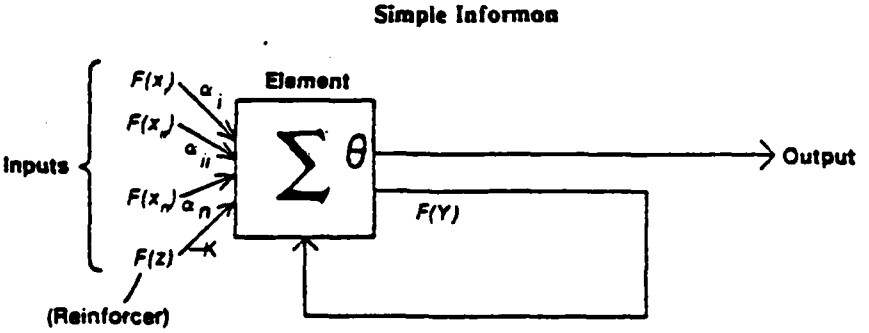


Fig. 7.6. The basic informon element. See text for further details. (After Uttley [1038].)

Figure 7.7 shows such an operation graphically and enables us to see how a particular choice of algorithm may or may not produce a stable change in weighting.

Uttley points out that analysis in the phase plane between change in α(i.e., $\Delta\alpha$) and α itself reveals the limitations of certain algorithms, notably those proposed by Hebb [397] and by Brindley [97] and Marr [646]. This is shown in Fig. 7.8.

> Hebb's postulate that an input causes an increased output simply indicates that if α is positive so must be $\Delta\alpha$. This postulate places the algorithm for acquisition within the right upper quadrant (++) of Fig. 7.8, but fails to specify a relationship or slope between variables $\Delta\alpha$ and α. Brindley [97] and Marr [646], in effect, consider a pathway with two states, one initial and one final, in which $\Delta\alpha$ and α increase together. With limiting values this reduces to an all-or-none, two state process. Without limiting values this represents an unstable system with positive feedback which will lead to regenerative explosion (line "a" in Fig. 7.8).* Uttley picks an algorithm which allows the values of $\Delta\alpha$ and α to fluctuate in the manner shown by lines "*b*" and "*c*" of Fig. 7.8 [1036].

System Normalization by Feedback of System State

Uttley points out that regenerative explosion may be avoided by introducing a normalization process, such as that of Malsburg [1047]. However, Malsburg's type of normalization shows an overly restrictive range of successful

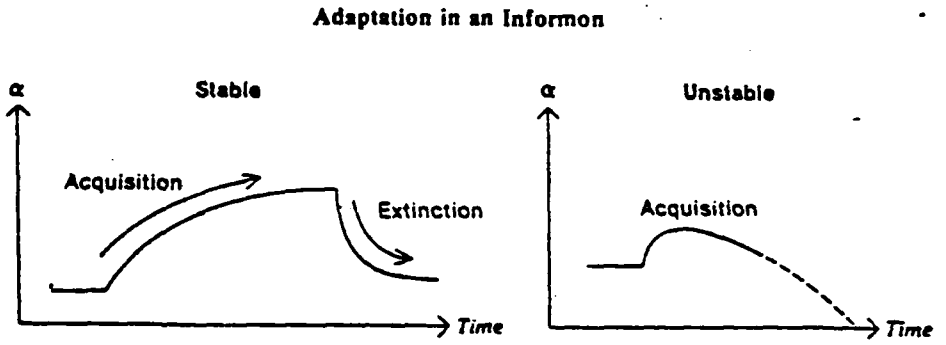


Fig. 7.7. Adaptation in an informon involves changes in α, the weightings of input, over time. In the example to the left an increase in α occurs during acquisition of input facilitation and a decrease occurs during its extinction or defacilitation. The parallel between this and conditioned behavior is deliberate. In the example to the right acquisition is an unstable process with α declining unintentionally past a certain transition point. This may occur because of failure to regulate the system state appropriately during the adaptive process. See text for further details about regulating the system state (After Uttley [1036].)

*This problem is avoided in some nonlinear systems that change state as levels reach certain limits.

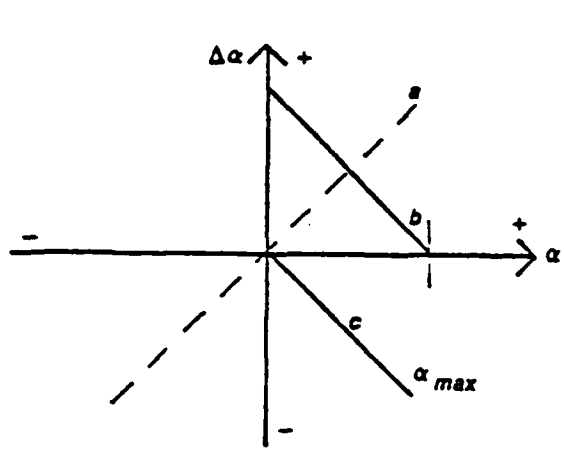


Fig. 7.8. Phase plane of α versus change in α (i.e., Δα). State changes along "a" such as those proposed by Marr [646] and Brindley [97] are unstable, while those along "b" or "c" are not. b mirrors the state change during acquisition in Fig. 7.7; "c" mirrors the state change during extinction. (After Uttley [1036].)

operation when applied to a system with positive feedback. To avoid this, Uttley turns to negative feedback as shown in Eq. 7.3b. Thus, the adaptation of his element, and probably some neuronal elements as well, depends critically on *negative feedback of information concerning the system state, F(Y).* Normalization results in part from the negative feedback of information concerning the system state (Fig. 7.9) and in part from the choice of adaptive algorithms described below (Eqs. 7.3a, 7.3b, and 7.5).

$$\Delta\alpha_i = -kF(x_i)F(Y), \tag{7.3a}$$

where $F(Y) = \Sigma F(x_i)\alpha_i$ and k is a positive constant.

However, this is still not enough to permit successful input discrimination, which depends additionally upon introduction of a reinforcing input.

Reinforcing Input

Reinforcement, or identification of the particular input $F(x_i)$ to be discriminated or enhanced by increasing α_i, is done by introducing a separate, labeling input $F(z)$ with α_z fixed and negative (Eq. 7.3b).

$$\Delta\alpha_i = -kF(x_i)\,[\Sigma_i F(x_i)\,\alpha_i + F(z)\,\alpha_z] \tag{7.3b}$$

Given an input $F(x_i)$, α_i will increase if $F(z)$ is present and will decrease if $F(z)$ is absent. With repeated reinforcement, α_i assumes the function of the acquisition curve shown in Fig. 7.7 (left) with $\Delta\alpha_i = \alpha_{max} - \alpha_i$ (line "*b*" of

Significance of Locus of Negative Feedback of Information Concerning System State Relative to Level at which the System State Becomes a Binary, All-or-None Output

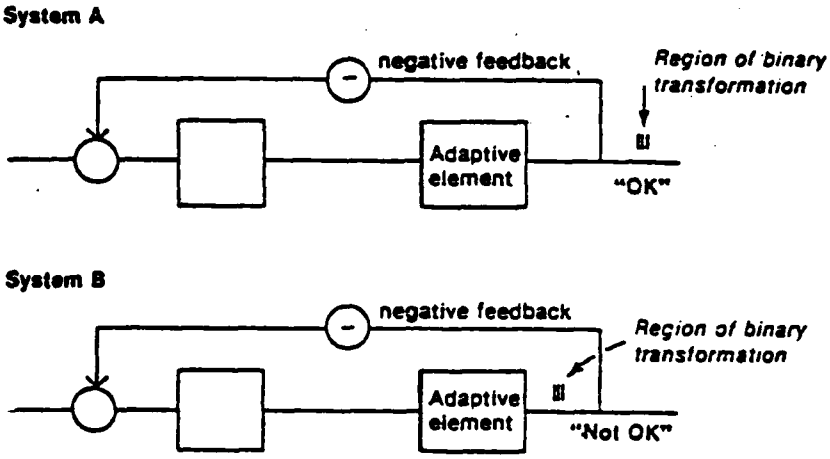


Fig. 7.9. By changing the locus of negative feedback so that instead of sampling the internal state of the adaptive element, as in (A), one samples only the binary output of the adaptive element, as in (B), one loses information required for normalization and an unsatisfactory adaptive process may ensue. The location of the binary encoder is shown by |||. *(Cf. Uttley [1033].)*

Fig. 7.8). Without reinforcement, α_i assumes the function of the extinction curve in Fig. 7.7 (left), with $\Delta\alpha_i = \alpha_i$ (line "c" of Fig. 7.8). Without a reinforcer, $F(z)$, a curve such as that shown in Fig. 7.7 (right) would be obtained.

The transfer properties of Uttley's adaptive element are designed then to simulate the S-shaped acquisition curve of conditioning plus its decrement during extinction. Considerable attention is also paid to controlling and limiting elemental adaptation by closed loop, negative feedback of the element's internal state. This variable provides a significant constraint on the operation of the adaptive element and may constitute a general requirement of successful self-organizing adaptive operations.

Mutual Information Constraint

Uttley imposes one further constraint on the operation of an informon, namely, that α be a modification of Shannon's mutual information function*:

$$\log \frac{P(x_i \text{ and } Y)}{P(x_i)\,P(Y)} = I(x_i{:}Y)$$

*see p. 381

This constraint can be applied to the operation specified in Eq. 7.3b. As a result:

$$\alpha_i = K[\ln F(x_i) + \ln F(Y) - \ln F(x_i)F(Y)]^* \tag{7.4}$$

or to simplify

$$\alpha_i = -KI(x_i:Y) \tag{7.5}$$

Thus, an increase in $F(x_i)$ will result in an increase in α_i; an increase in $F(Y)$ will also increase α_i, but an increase in $F(x_i)\,F(Y)$ will decrease α_i.†

In summary, parallel processing systems with adaptive elements appear to handle discrimination tasks quite easily. Hierarchically organized networks, such as pandemonium, with non-uniform elements and specialized adaptive properties can handle some forms of learning with particular ease, but may cling tenaciously to errors in discrimination arising from their particular design. (This erroneous "behavior" is not unlike that of perseveration and neglect described in Chapter 6.) Other automata, such as the informon, may rely on optimized properties of more uniform adaptive elements. As Uttley has shown [1036-1038], the adaptive weightings must change in ways that are nonexplosive. Introduction of negative feedback of information concerning the state of the controlled system can contribute to a normalization process which, in turn, can reduce the possibility of explosive change. Other features such as relaxation of increased weighting and discriminative control of the weighting changes of certain inputs require additional features. These may include particularized dependencies between inputs such as the mutual information feature of Uttley's model or labeled reinforcing inputs such as $F(z)$ of Uttley's model.‡

By slightly redefining Uttley's circuits (Fig. 7.10), it is possible to form closed loop, positive feedback pathways that might support motor labeling in classical, associative conditioning (see Chapter 3). Positive feedback would augment a particular message of motor significance transmitted within a specific, closed loop circuit. The augmented message would facilitate the formation of adaptations along the pathway. Another mechanism (e.g. inactivation) would be required to avoid explosive change.

Further support for a possible role of positive feedback in neural control systems is furnished by Freeman's model of olfactory bulb circuitry [299]. In that model, the effect of the stimulus is to increase feedback gain in an ensemble of neurons that are receptive to the stimulus. "If a local ensemble containing sensitized subsets that are mutually excitatory is excited, the basis exists for a regenerative increase in activity in response to an adequate stimulus" [299]. The model has five main features:

*a simplification; properly, the equation incorporates the ensemble average of the frequencies of signal occurrence. See Uttley [1036].

†Further material concerning these equations can be found on pp. 381,382.

‡For further particularizations of interest, see Uttley, A. M. *Information Transmission in the Nervous System.* London: Academic Press, 1979.

Feedback of Motor Labeled Information

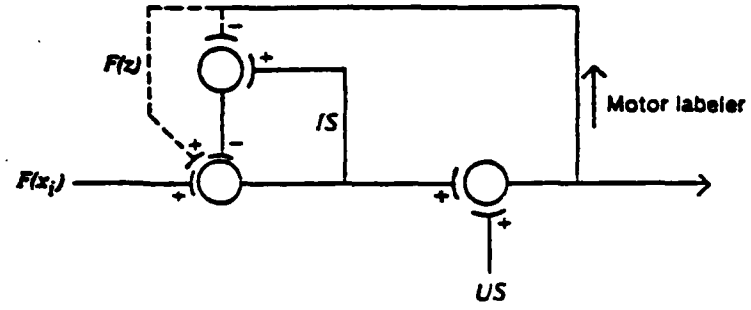


Fig. 7.10. Schema for motor (M) labeled reinforcements derived from Uttley's informon model. The US activates neurons which act directly (or indirectly) as the F(z) input. Selective labeling of the "upstream" neurons which project, selectively, to the activated units is potentiated because of positive feedback within the circuitry. For this schema to operate successfully, some feature such as local recurrent inhibition would be required to monitor the system state and prevent explosive buildup from the positive feedback. IS=feedback of information concerning internal system state.

1. A nonlinear signal range that is near linear about the origin.
2. Bilateral saturation with gain approaching zero at both extremes of wave amplitude (this feature provides stability).
3. A 2:1 asymmetry of the asymptotes of the circuit transfer function (arising from the features of the olfactory bulb and cortical electrophysiology on which the system is modeled).
4. A gain that increases with positive (excitatory) input.
5. A gain that is modifiable in a pattern that depends on background or steady state activity, which in turn is presumed to be under centrifugal control.

The positive feedback should satisfy three constraints for stability: (1) the regenerative effect should not be unduly perturbed by noise, (2) it should be self-limiting in maximal amplitude, and (3) it should be rapidly self-terminating to permit additional inputs to pass [299].

Analysis

Analysis of the organization of systems as complex as the brain need not be considered impossible when systems involving complex communication (television), learning (computer automata), elaborate control mechanisms (guided missiles), and even uncertainty (the atom) have proved amenable to analysis. It is possible, in principle, to analyze a complex system if it is finite, obeys the laws of physics, and meets the constraints of the analytic method.* This

*One should never underestimate the importance of this latter consideration (see pp. 322-401 and Epilogue).

is so irrespective of whether the system is biological or mechanical. Means exist, such as linear systems analysis (p. 366), for partitioning many complex systems into relevant suboperations that are easier to analyze, and some neural systems are amenable to this form of partitioning [429,1103,1123]. Other means such as flow graph techniques (p. 368) can be used to analyze neural network operations on a cell to cell basis despite complex interrelationships including feedback between receptor and effector functions. Finally, means can be found, as by computer simulations, to reassemble and test the analyzed component functions with reference to the overall organization of the network.

Apart from complexity, another objection that is frequently raised to analyzing brain function is that general physical theories comparable to those found in chemistry or other basic disciplines are lacking. While it is true that theories of information handling are not so advanced as those in other fields, the existing theories have been found applicable to predictive treatment of information handling by real systems. The usefulness of Shannon's information coding theories in the communications industry is well established and has been complemented by the emergence of additional theories in the areas of systems control. The challenge for neuroscientists is to develop extensions of the above theories that are applicable to treatment of specific neural information processing systems. The basic purpose of the material that follows is less ambitious, being simply to outline some of the potentially relevant analytic methodologies.

Signal Analysis

The fundamental idea of Wiener and Lee's approach to analysis of communications systems is that messages, signals, and noise should be considered statistically and described in terms of probability theory [582]. Messages are information carrying functions, i.e. member functions in an ensemble, or numerically large aggregate, of signals (relevant information) *and* noise (irrelevant information) and their combination. Communication theory has led to analysis of linear message-transmission systems using convolution as the basic analytic device. Given a linear system (p. 396) and consideration of signals and noise as random processes [582], signal analysis can be performed by time series analysis utilizing (1) Fourier series, (2) power spectral density, (3) correlation, and (4) convolution (Table 7.2).

Most signals to be analyzed within the CNS are changes in voltage or current as a function of time. To determine the structure of a signal, it is analyzed in terms of its frequency components (c.f. Figs. 5.30, 7.11, 7.12, and 7.14). The signal may be described in terms of its *major* frequency components (Figs. 7.11, 7.12) or, more precisely, in terms of the power consumed across a 1 ohm resistor by passage of the different frequency components of the signal (including harmonics). The latter is called the power spectral density (Fig. 7.14). Some information, that concerning the phase of one frequency component

* * * * * * * * * *

Control of Adaptive Systems

Linear systems analysis admits a general theory of adaptive control provided that the system is linear and the usual constraints are satisfied. One constraint is that the result of adaptation depend on the entire past history of adaptation within the system. Another is (usually) that the transfer function of the system be time invariant.

When using this theory, adaptation is introduced as a controller function, $g(t)$, as in Fig. 7.24. It operates *by adding an additional input to the system* much like $F(Y)$, the negative feedback of the system state, in Uttley's informon. It does not directly modify the original system transfer function, $H(t)$. To do the latter would lead to a time-variant or self-organizing adaptive system which could easily be nonlinear and, therefore, not amenable to analysis by this theory.

For a linear system with the feedback circuit shown in Fig. 7.24(A), the output, $Y(t)$ is a function of the input, $X(t)$, the system transfer function, $H(t)$ and the controller function, $g(t)$. If the LaPlace transform, $F(s)$, of each function is taken,

$$\text{e.g., Output } F(y) = \mathcal{L}\, Y(t) = \int_0^{\infty} Y(t)e^{-\mathcal{L}t}dt, \qquad (7.49)$$

(note relationship to Fourier transform, Eq. 7.6), then, for a linear system,

$$\text{where} \qquad f_1 * f_2 = F_1(s)\,F_2(s), \qquad (7.50)$$

i.e., in the absence of a control loop,

$$F(y) = F(x)\,F(h). \qquad (7.51)$$

The output of the linear system with *negative* feedback (Fig. 7.24A) may therefore be expressed as

$$F(y) = \frac{F(h)\,F(x)}{1 + F(h)\,F(g)} \qquad (7.52)$$

For the feedforward circuit shown in Fig. 7.24(B),

$$F(y) = 1+F(g)\;\; F(x)\,F(h) \qquad (7.53)$$

assuming *positive* feedforward.

One may wish to consider the linear control circuits of Fig. 7.24, the designs of automata shown in Fig. 7.5, and the algorithms of adaptation listed on p. 395 in relation to the descriptions of control systems that follow.

Control Systems

Several types of control systems are recognized, each with its own critical feature(s). For example, there are:

Control systems:

1. With or without memory.
2. With or without set point variance.
3. With or without self-organizing adaptation.
4. With open or closed loop control.
5. With feedforward or feedback control.

The list is by no means complete or (in considering how to classify different types of switches, flywheel governors, thermostats, and innate or learned behaviors) are all of the differences unique or mutually exclusive.

Adaptations involved in control may reach some maximum or minimum value, or may proceed at some steady state level with or without range bounding as was described earlier (Figs. 7.7, 7.8).

Open Loop Adaptive Control Systems

An open loop control system receives no feedback information regarding the state of the adaptive system. There may be indirect feedback of information (e.g., from the environment and changes therein caused by the system's operation) to support the predetermined system operation, but not to cause the controller to adapt. Control is exercised entirely by predetermined adaptations based on the detection of predefined contingencies. Thus, in a thermostat adaptation occurs on the basis of temperature detection plus a prespecified contingency (if the temperature is low, turn on the heat; if high, turn it off). There is no feedback to alter the rules of adaptation based on past performance. There is instead an input of ambient temperature and a fixed course of adaptation contingent on its level. Neuronally, open loop adaptation may be contingent on two different synaptic inputs occurring together, as with heterosynaptic facilitation and inhibition.

Open loop control systems will typically have great stability since their adaptive features are entirely predetermined. However, it may be difficult to achieve a control operation of high sensitivity with an open loop system. This is because the accuracy of control depends on the system's initial calibration and on the precision of the involved components. The operation of open loop control systems will be vulnerable to component breakdown or interference from outside noise that was unanticipated in their original control design. Driftage away from the initial component set point is uncorrectable with an open loop control system. There is also no possibility for self-organizing adaptation, since there is no regard for the present or past system state.

Closed Loop, Feedback Control Systems

A closed loop control system normally uses feedback concerning the value of a controlled variable or the state of the adaptive control system, as a means to control further adaptation. In a closed loop, self-organizing control system, the response of the modified element should have a direct effect on the

control action (Fig. 7.24A). This circuit may be compared with that of a feedforward control system (Fig. 7.24B) in which information from the input modifies the controller without regard to the system state.

Either feedback or feedforward circuitry can be used to reduce the error or improve the response time of linear control operations, such as described earlier, and the circuitries may be either positive or negative. Because of the closed loop operation, feedback may have self-potentiating effects when it operates either as a supplemental control input to the system or as a self-organizing modifier of the system's original transfer function. Positive (regenerative) feedback is distinguished from negative (degenerative) feedback in that the former augments the gain of the loop system and can lead to explosive buildup. *Positive feedback* returns an output to the input so as to add another, positive input. This will permit rapid change or increased sensitivity of the system by which transforms between input and output are performed; however, it also tends to unstabilize the system and increase distortion of the signal input. *Negative feedback* returns the output to the input in such a way as to add another, negative input. Negative feedback then decreases the gain of the loop system and can lead to damping or a cut off of signal transmission. This tends to stabilize the transfer between input and output and reduce distortion, although the sensitivity and rapidity of the transfer operation may be reduced.

Negative feedback control systems have a system response that is relatively insensitive to brief external disturbances and to internal variations in parameters of the operations controlled. This is because the output, e.g., $F(y)$ in Eq. 7.52, approaches $F(x) \div F(g)$ if $F(h)\,F(g) \gg 1$. Thus, small deviations in component operations or even the original control parameters may not overly disturb the control system, provided that their manifestations are accessible to the control loop. This permits relatively noisy components to be used for the system operation. Note, however, that when a closed loop system is

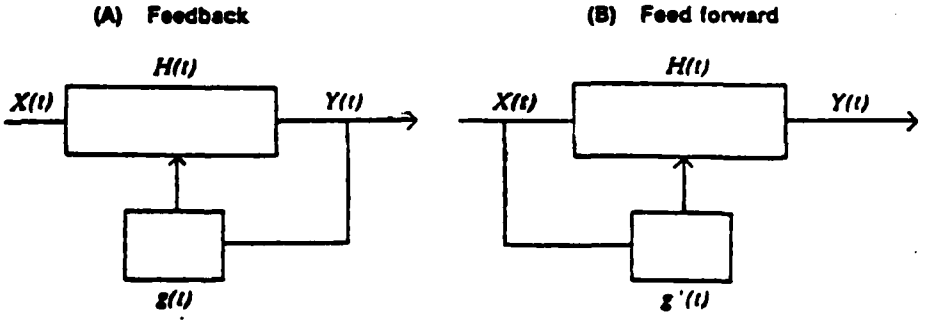


Fig. 7.24. Linear systems with feedback control (A) and feedforward control (B). The systems have input X(t), transfer function H(t) and output Y(t). g(t) and g'(t) are the controller functions. Differences between applying the output of the controller function as an "extra" (additive) system input versus applying it to direct adaptation of the system transfer function are discussed in the text.

carrying a range of frequencies over the feedback path, the frequency characteristics of the network may become an important source of error. At one frequency the phase of the signal fed back may be such as to produce negative feedback, but at another frequency the phase relationships may be such as to cause positive feedback, and oscillations may occur. Stability of control can therefore be a problem with closed loop control operations, since with closed loop adaptive control, there may be oscillating errors of overcorrection leading to explosive instability or drift in an undesired direction. The latter feature, taken in a converse manner, lends itself to self-organizing adaptive control, provided that some means be found to avoid maladaptation.

Some typical characteristics of closed loop systems which may be of interest with regard to their possible use in the design of self-organizing systems are as follows:

1. Some stable closed loop systems tend to have a transient response performance which can be predicted from the steady-state, closed loop plot of magnitude versus frequency (e.g., Nyquist plot).
2. A system designed for optimal steady-state operation may have unstable transient characteristics.
3. Self-organizing adaptive systems, i.e., control systems that incorporate time-variance based on system operation into the adaptive scheme, must have some means of evaluating how well the control operations are being performed. This index of performance must be reliable and unambiguous with respect to the optimal range of operation.
4. It should be possible to obtain a performance index without disturbing the operation of the system and in a form which is amenable to insertion into that part of the system in which control of adaptation is accomplished.
5. If hill-climbing techniques are used to control steady-state adaptation [e.g., 883], false peaks must be defined and avoided.

Other Mathematical Techniques

The two theories that follow are introduced because of their promise for advancing our ability to analyze complex adaptive networks. Their mention is abbreviated because of their novelty and because so little is known at present about their proper application.

Ergodic Theory

Ergodic theory "is concerned with the average behavior of large collections of molecules that move randomly for indefinite periods of time . . . Ergodic theorists commonly deal with measure and probability spaces and have developed powerful theorems involving ramification of these ideas [537]." The reader is referred to Kolata [537] for further discussion of ergodic theory.

Field Theory

"Field theory, as elaborated by Weiss, Wolpert, and others," indicates that a field "can be defined operationally as a domain within which changes in the

presumptive fates of cells can occur" [300]. Cells may be assigned positional values according to their physical locations in the coordinate system of a particular field. In terms of positional information theory, the field can be defined as a set of cells which have their positions specified with respect to the same coordinate system. Further information is available elsewhere [300].

Specific Theories of Line Labeled Information Handling

A Geometry of Perception–Processing of Sensory Labeled Information

Minsky and Papert [672] have uncovered the beginnings of a powerful mathematical theory concerning a geometry of perception pertaining to the processing of sensory labeled information. The theory also deals with adaptive features of the processing. The topologic transformation of problems of image recognition and perception into problems of line labeled geometry is insightful and potentially more useful than these authors may have imagined originally.

As shown in Fig. 7.25, image processing involves sets of receptive elements that receive and process aggregates of sensory labeled information. Each unique, sensory labeled set independently processes its sensory aggregate according to some function, φ_i. The results of processing by each set are combined by means of a function Ω to obtain the value, ψ. The problems to be resolved are:

1. How can arrays of this sort be organized to permit a particular $\psi(X)$ to be a useful designator of a particular input, X, at the receptor elements?
2. Can a geometry be devised that will describe this process precisely and define some reasonably optimal approach to this problem?

Minsky and Papert begin their solution of these problems by pointing out that some meaningful restrictions must be placed on the function Ω and the set Φ of functions $\varphi_1, \varphi_2, \ldots, \varphi_n$ if the geometry is to be useful. And they point out that previous treatments of this type have been more anecdotal than mathematical.

It is also desirable to introduce variable weighting or some other potential means of adaptation, into the analysis. As shown in Fig. 7.26, weightings $\alpha_1, \alpha_2, \ldots, \alpha_n$ may be assigned each function $\varphi_1, \varphi_2, \ldots, \varphi_n$.

In addition, Ω may be replaced by a summation or integration function, Σ, and a threshold detector, θ, may be added to designate a particular value or region of ψ. When α is variable, this constitutes a simple perceptron, named after the automata of this general type that were designed by Rosenblatt [838-841]. It is noted by Minsky and Papert that in such automata α tends to grow faster than Ω in adaptive processing operations requiring memory storage.

The more complex perceptron admits multiple, redundant inputs as shown in Fig. 7.27. This type of processing of sensory labeled information corresponds closely to that carried out by the nervous system and is amenable to analysis by means of the Group Invariance Theorem.

A Simple Image-Processing Automaton

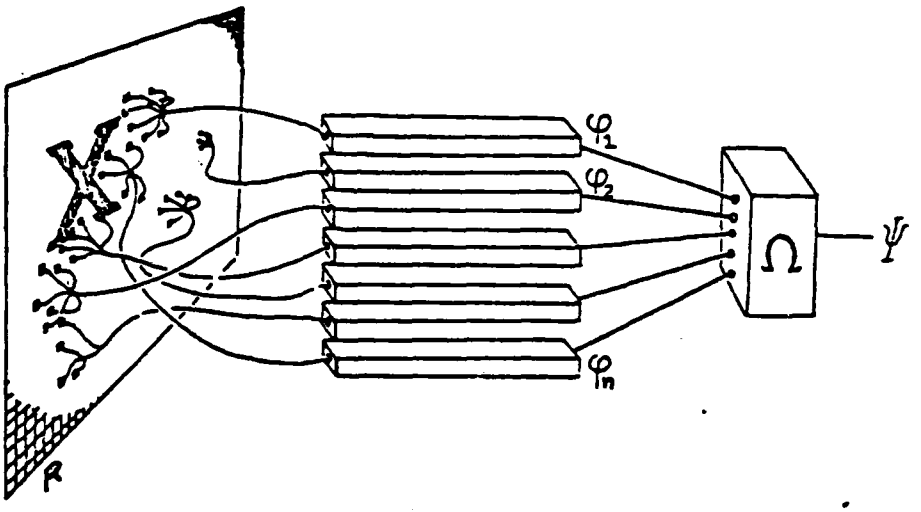


Fig. 7.25. An example of simple, multiple channel, image processing. See text for further details (From Minsky and Papert [672].)

Group Invariance Theorem

The Group Invariance Theorem of Minsky and Papert permits analysis of perceptron operations (i.e., the geometry of sensory image processing) by algebra instead of statistics. This theorem examines the relationship between all possible receptor activations (all sets of sensory labels, $r_1, r_2, \ldots, r_n$) and their representation across a theoretical space of $\alpha_{\varphi}\varphi(X)$ for $\varphi \epsilon \Phi$.

A Perceptron

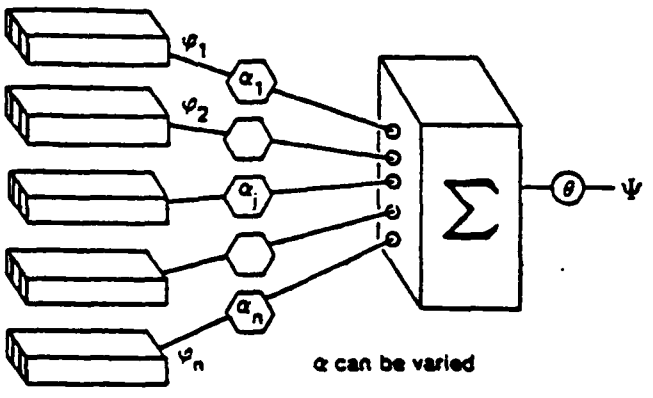


Fig. 7.26. Elementary perceptron (α can be varied). (From Minsky and Papert [672].)

Equivalence Between Parallel Processing and Group Invariance Theorem

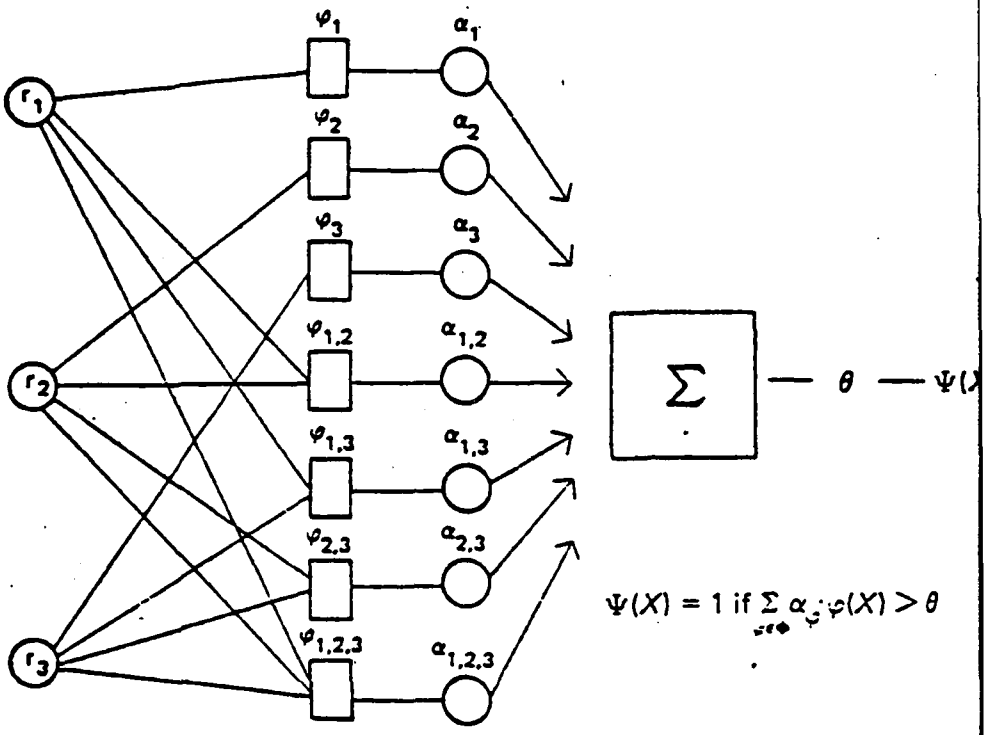


Fig. 7.27. A perceptron reduced to Group Invariance Theorem coefficients. (From Minsky and Papert [672].)

In effect, the Group Invariance Theorem permits an algebraic analysis of all geometries of rearrangements (or representations) of the original set of possible receptor labeled activations. It allows determination of which aggregates of $\alpha_\varphi \varphi(X)$ (or values of ψ) reflect a unique transformation of the group of possible transformations of the space of the receptor labelings, $r_1, r_2, \ldots, r_n$, upon the predicates, $\varphi_1, \varphi_2, \ldots, \varphi_n$.

Given any predicate φ and group element g,* Minsky and Papert define φg to be the predicate that, for each X, has the value $\varphi(X)$. Thus, one will always have $\varphi g(X) = \varphi(gX)$. Φ will be said to be closed under G if for every φ in Φ and g in G the predicate φg is also in Φ. If a perceptron predicate is invariant under a group, G, then its coefficients need depend only on the G-equivalence classes of their φ's [672].

The Group Invariance Theorem states that if:

(i) G is a finite group of transformations of a finite space, R;

*Given a group G, two figures, M and N, are G-equivalent if there is a member g of G for which $Mg = N$.

(ii) Φ is a set of predicates on that space closed under G;
(iii) ψ is in L (Φ) and invariant under G. Then, there exists a linear representation of

$$\psi = [\sum_{\varphi \epsilon \Phi} \beta_\varphi \varphi > 0]$$

for which the coefficients β_φ depend only on the G-equivalence class of φ, that is if $\varphi \underset{G}{\equiv} \varphi'$ then $\beta_\varphi \equiv \beta_{\varphi'}$.

$L\ \Phi$ is the set of all predicates for which ψ is a linear threshold function with respect to Φ, and a predicate is a function that has two possible values, i.e., a binary function. ψ is a linear threshold function with respect to Φ, (φ is in $L(\Phi)$, if there exists a number θ, and a set of numbers, α_φ one for each φ in Φ, such that:

$$\psi(X) = [\sum_{\varphi \epsilon \Phi} \alpha_\varphi \varphi(X) > \theta] \,. \qquad (7.54)$$

Restrictions on Perceptron Operations and Limitations in Geometric Patterns That Can Be Recognized

Perceptrons are not without restrictions in the types of operations that can be performed and the geometric patterns that can be recognized.

Restrictions of Geometry. The perceptron operations discussed by Minsky and Papert have a receptor geometry restricted as follows:

1. The number of points (or receptive elements) is limited. Hence, the predicates of the points are of limited order.
2. The distances between points are restricted. Hence, their predicates are diameter-limited.

Order has to do with the number of characteristic variables needed to represent a set of particular functions. For example, the order of ψ is the smallest number, K, for which a set Φ of predicates can be found satisfying:

$$|S(\varphi)| \leq K \quad \text{for all} \quad \varphi \text{ in } \Phi, \quad \psi \epsilon L(\Phi)$$

where $S(\varphi)$ is that subset of receptors, $r_1, r_2, \ldots, r_n$, upon which $\psi(X)$ (the set of functions required for recognizing X) really depends, and $L(\Phi)$ is the linear threshold function of Φ, the set of all predicates that can be defined by Eq. 7.54.

Linear threshold function perceptron operations are of order 1. So are all the Boolean functions of two variables except for:

i. Exclusive-or ($XY' + X'Y > 0$) and
ii. Its complement identity, $X \equiv Y$ ($XY + X'Y' > 0$)

which are of order 2.

Type of Processing Operations. Perceptrons are particularly good at doing processing operations of the types called "local" or "conjunctively local" by Minsky and Papert [672]. By local is meant that all tests (analytic or logical) can be done independently and the final decision can be made by a logically simple procedure such as unanimity of all tests.

A predicate, ψ, is conjunctively local of order K if it can be computed by a set Φ of predicates φ such that:

i. Each φ depends on no more than K points of the space R;

ii. $\psi(X) = \begin{cases} 1 & \text{if } \varphi(X) = 1 \text{ for every } \varphi \text{ in } \Phi \\ 0 & \text{otherwise.} \end{cases}$

Such processing will enable a perceptron to distinguish convex from nonconvex figures at the receptors by the test that if there exist three receptor points, p, q, and r, such that q is in the line segment joining p and r, and

$$\begin{aligned} p &\text{ is in } X, \\ q &\text{ is not in } X, \\ r &\text{ is in } X, \text{ etc.} \end{aligned}$$

then the set X is not convex (Fig. 7.28). Thus, $\psi_{\text{convex}}(X)$ is conjunctively local of order 3 by application of this three-point rule [672].

Interestingly, the determination of connectedness between points can be shown not to be conjunctively local of any order in a diameter-limited perceptron processing operation. Hence, perceptrons of this type cannot compute connectedness of geometric figures whereas they can compute convexity. However, as inspection of Fig. 6.6C will indicate, we, too, have our difficulties in determining connectedness.

Types of Perceptrons

Given that "a Perceptron is a device capable of computing all predicates which are linear in some given set Φ of partial predicates" [672], five different types of perceptrons can be distinguished. They are:

1. *Diameter-limited Perceptrons*—the set of points upon which each φ depends (for each φ in some given set Φ) is restricted not to exceed a certain fixed diameter in the plane.

2. *Order-restricted Perceptrons*—a perceptron has order $\leqslant n$ if no member of Φ depends on more than n points.

3. *Gamba Perceptrons*—each member of Φ may depend on all the points but must be a linear threshold function, with each member of Φ itself being computed by a perceptron of order 1. Thus,

$$\varphi_i = [\sum_j \beta_{ij} r_j > \theta_i]$$

(each φ_i is a threshold perceptron of order 1) and

Determination of Convexity by Three-Point Rule

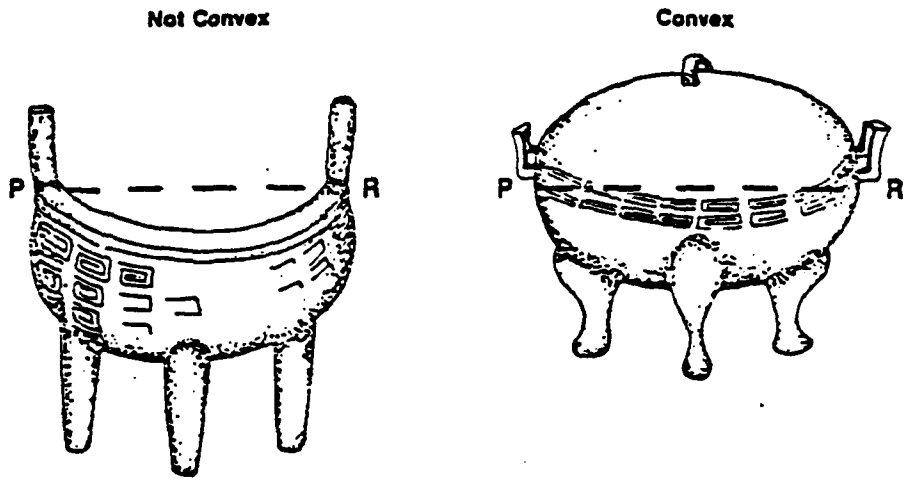


Fig. 7.28. Determination of convexity by three-point rule [672]. Draw a straight line connecting surface points such as P *and* R. *If a third point, taken anywhere along this line, is inside the space of the object, the surface is convex.*

$$\psi_{\text{gamba}} = [\sum_i \alpha_i [\sum_j \beta_{ij} r_j > \theta_i] > \theta] \tag{7.55}$$

The Gamba perceptron is thus a two-layered perceptron. Note, however, that no improvement is afforded by any multi-layered system, without loops, in which there is an order restriction at each layer wherein only predicates of finite order are computed.

4. *Random Perceptrons*—the φ's are random Boolean functions. They are order-restricted and Φ is generated by a stochastic process according to an assigned distribution function (cf. Rosenblatt [838-841]).

5. *Bounded Perceptrons*—Φ contains an infinite number of φ's, but all the α_φ lie in a finite set of numbers [672].

Size, Speed, and Layer-Hierarchy Considerations in Perceptron Operations

Given application of the group invariance theorem to analysis of perceptrons of the above types, several observations may be drawn concerning effects of size, speed, and layer or hierarchy of operation.

First, using more "memory" does not seem to advance the kinds or efficiencies of linear threshold operations that are performed. This is interesting because many believe that adding memory will greatly improve the types of

operations that can be performed. Minsky and Papert would suggest that design is more important than size.*

Second, it should be possible to specify connection-matrices between elements that will optimize the efficiency of processing vis-à-vis the number of elements involved. Examples of different connection matrices are shown in Fig. 7.29.

Multilayer Perceptrons with Loops

According to Minsky and Papert, the group invariance theorem cannot be applied to multilayered perceptrons with loops.† The addition of loops thus reopens analytic questions. It remains to be seen how the addition of loops limits general theories of sensory information processing by perceptron-like automata.‡ Some analytic questions can be answered a priori. For example, the use of loops in processing will not improve the speed of computation afforded by loop-free serial processing. Other questions cannot. Thus, it is unclear whether or not loops afford the possibility of more complex analytic operations. Given finite order processing, a prerequisite for mathematical analysis, it is questionable whether loops afford any order-improvement beyond that possible with a hierarchical multilayered construction.

What loops do offer is the possibility of using the simple feedback principle for "training" or error correction. Minsky and Papert believe that the perceptron convergence theorem provides analytic proof that where such "learning, adaptation or self organization does occur, its occurrence can be thoroughly elucidated (mathematically)" [672].

A Geometry of Sorting—Treatment of Motor Labeled Effectuation, Synthesis, and Decision Making

Comparison of Fig. 7.30 with Fig. 3.42 will disclose how motor-labeled effectuation or decision making is implicit in the design of perceptrons.

What has not been treated explicitly in the course of analysis of perceptron operations is the geometry of sorting, i.e., an algebraic analysis of motor labeled effectuation comparable to that for sensory reception presented earlier. Three positions are possible. One is that this geometry is completely implicit in the classification algorithms described by Minsky and Papert (perhaps as a substructure of predicates). The second is that significant extensions of their algorithms and theory need to be made—perhaps by an expanded treatment of conditional probabilities and Markov processes.¶ The third position, that such

*It is not yet clear if artificial intelligence performed by a large, specifically designed computer (capable of "logical" operation) can adequately simulate intelligence based on *unincorporated* design features. Logic may be used to approximate the needed features, but the results may be unsatisfactory and the errors difficult to detect, as in some of the phenomena illustrated in Chapter 6.

†Although it will be recalled that closed flowgraphs, consisting of loop circuits, *can* be solved.

‡Also, some loops can be eliminated by use of flowgraphs.

¶Another class of algorithm that can compute connectedness may be required—Turing machines can compute connectedness; perceptrons cannot.

Connection-Matrices

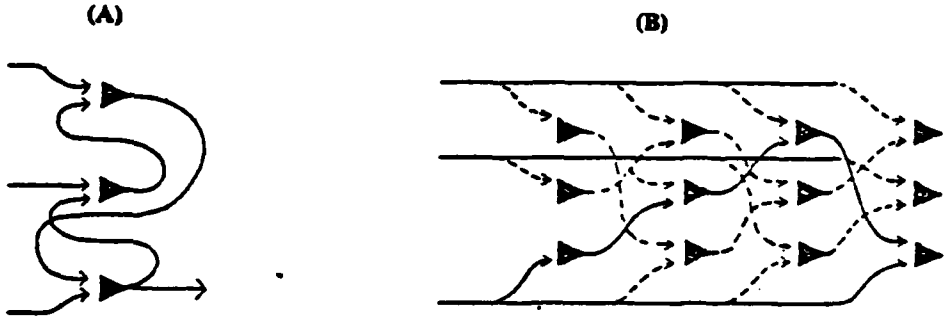


Fig. 7.29. Different connection matrices. Are those in (A) equivalent to those darkened in (B)? (There is feedback in A.) Are some elements and connections in B superfluous? (Even if different transfer functions of several elements could be combined, the connections would allow unique dependencies between inputs, elements, and outputs). (Sketches after Minsky and Papert [672].)

A Learning Machine

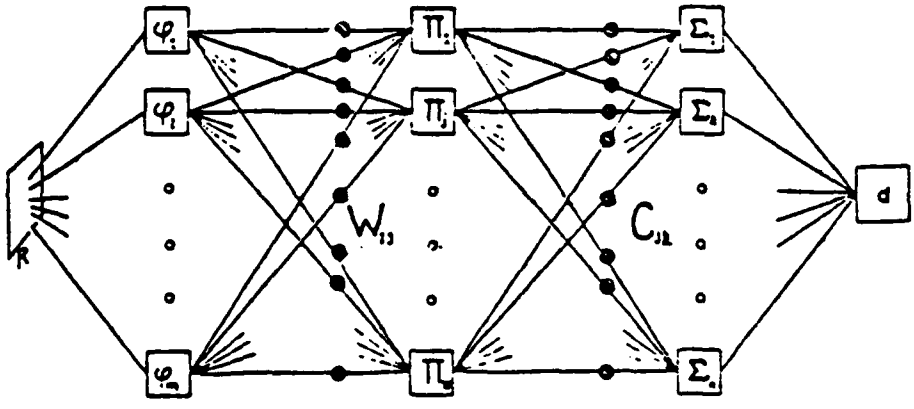


Fig. 7.30. A multilayer perceptron capable of making decisions (d). (From Minsky and Papert [672].) The adaptations controlling Δw_{ij} and Δc_{jk} might benefit from feedback of information concerning the system state.

a geometry and analysis is unrealizable, may be dismissed if one accepts Minsky and Papert's view that workable systems are subject to analysis and this author's assertion that such systems are visible within the reflex pathways of the nervous system.

Classification Algorithms

The following classification algorithms for separating different sensory labeled aggregates at d in Fig. 7.30 have been suggested by Minsky and Papert [672].

1. *Perceptron convergence theorem.* Let F be a set of unit-length vectors. Let $A \cdot \Phi$ be the vector notation of $\Sigma \alpha_\varphi \varphi(X)$. If there exists a unit vector A^* and a number $\delta > 0$ such that $A^* \cdot \Phi > \delta$ for all Φ in F, then a simple program (see Minsky and Papert [672], p. 167) can be devised that will converge in a finite number of iterations on a separation of all $\Phi \in F$. A variation of this program (see [672]) will separate more than two classes of input figures: $F_1, F_2, \ldots, F_n$.

A limitation of this classification algorithm is that only linear separations are performed optimally by this method.

2. *Bayes' linear statistical procedure.* Again, let F be a set of unit-length vectors, with one vector, A_i^* such that $A_i \cdot \Phi > \delta$ for all Φ in F. If $A_j = (\theta_j\, \omega_{1j}, \omega_{2j}, \ldots)$,

$$\text{where } \omega_{ij} = \text{Log}\left(\frac{P_{ij}}{1-P_{ij}}\right)$$

and P is the probability that $\varphi_i = 1$, given that Φ is in F_j, then $\Phi \in F$ will be separated with the lowest possible error rate, given that the φ's are statistically independent. (This is, remarkably, a linear formula that can perform non-linear separation.)

3. *Best planes procedure*—This is essentially an error-minimizing tracking procedure whereby the set of A's is used for which choice of the largest $A_i \cdot \Phi$ gives the fewest errors. The presence of false peaks in hill-climbing searches by this method may limit its applicability.

4. *Cluster analysis*—Techniques are used to minimize the least square distance between different points in the receptor array (R) reflected by the different $A_i \cdot \Phi$. In effect, separation is performed on the basis of spatial clustering of each sensory aggregate. A more complete description of this approach and a cluster-analysis convergence theorem, with proof, can be found in Minsky and Papert's book [672].

5. *Exact matching or best matching*—This approach requires a large memory and is cumbersome. Each Φ that has ever been encountered, together with the identity of its associated F-class, is stored. New inputs are "recognized" on the basis of match against the store contents. With exact matching, a tedious search results in a solution with no errors. With

*denotes unit vector

"best" matching, a completely different type of procedure (e.g., algorithms such as those incorporating matched filtering—see Woody [1103]) is used to optimize signal detection, minimize errors, and reduce search time (see [672,704,1123]).

Probability as a Descriptor of Motor Effectuation: The Conditional Probability of Sorting. An Algebra of Events

Just as entropy is relatable to the uncertainty of configurations of gas molecules in a dimensional space, and provides some measure thereof, so does probability provide a measure or index of the likelihood of events. As we have seen from the work of Boltzmann and of Shannon, the events may be physical-chemical or they may be informational-probabilistic.

Just as chemical events may be described as occupying a space [328], so may other probabilistic events be described in terms of the space they occupy. The space of probabilistic events is described by set theory and Venn diagrams thereof. The sample space (Fig. 7.31) represents the number of possible different arrangements of sample points or outcomes, and each event or specific outcome in the sample space can be assigned a probability of occurrence.

Set theory is described by a set of axioms that fully define the algebra of events [cf. 240]. With respect to Fig. 7.31, they are:

1. $A + B = B + A$ (commutative law); also for multiplication, $AB = BA$
2. $A + (B + C) = (A+B) + C$ (associative law); also for multiplication, $A(BY) = (AB)Y$
3. $A(B + C) = AB + AC$ (distributive law)
4. $(A')' = A$ (' = "not" or the complement of whatever it follows)
5. $(AB) = A' + B'$
6. $AA' = \Phi$ (Φ = complement of U)
7. $AU = A$ (U = union of two events—the collection of all points in either or both event spaces)

This set of axioms is also the set of constraints by which linear systems are bound and defined.

Simple Probability. Could probability be used to describe motor effectuation, i.e., the motor events (or decisional space) possible as outcomes of a particular network? If so, could some general formulation be derived, comparable to the group invariance theorem to permit a general algebraic treatment of the geometry of sorting or motor effectuation? The answer to the first question is yes; the answer to the second, perhaps. The sample space, S, of possible motor outcomes is made up of a number of points, $E_1, E_2, \ldots, E_n$. Each point, E_k, has an expected probability of occurrence $P(E_k)$.*

The probability of occurrence of event A, $P(A)$, is the sum of the probabilities of all points within it. The sum of the probabilities of occurrence of all points equals 1, which is equal to the probability of the entire sample space. Thus, $P(A)$ must be between 0 and 1.

*Event A may be mapped from sets of $P(E_k)$.

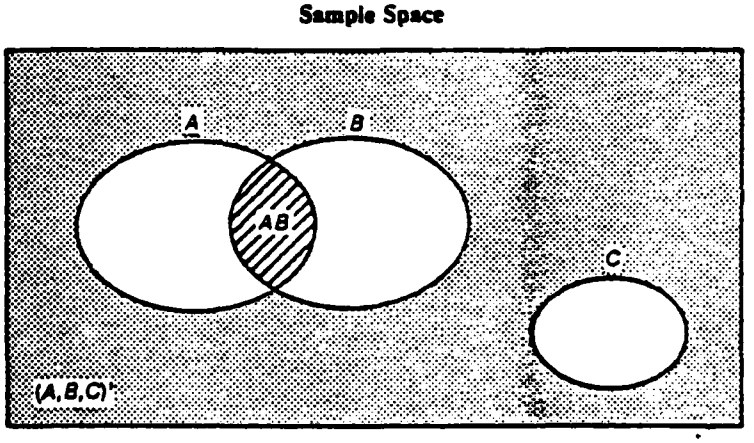


Fig. 7.31. The sample space of A, B, C *and* (A,B,C)'.

Conditional Probability. Conditional probability deals with the probability of an event A occurring given that some other event B has just occurred. If the events are completely independent, the probability of event A occurring will be equal to the general probability of occurrence of event A, $P(A)$. If there is some dependency, the probability of event A occurring, once B has occurred, may be different from the general probability of occurrence of event A. Bayes has systematized this relationship. If one thinks of B as the causal event and A as the affected event, the probability that A occurs given that B has occurred, $P(A/B)$, is equal to the general probability of occurrence of A, $P(A)$, times the probability of the effect B given that the phenomenon A has occurred, $P(B/A)$, divided by the probability of event B, $P(B)$. Thus:

$$P(A/B) = \frac{P(A)\,P(B/A)}{P(B)}. \tag{7.56}$$

Interestingly, this theorem may be generalized to encompass the relationship of a set of events $A_1, A_2, \ldots, A_n$. This is because $P(B)$ will equal $P[(A_1 + A_2 + \ldots A_n)B]$ or $\Sigma P(A_iB)$.

Thus,

$$P(B) = \sum_{i=1}^{N} P(A_iB) \tag{7.57}$$

It can be shown that:

$$\sum_{i=1}^{N} P(A_iB) = \sum_{i=1}^{N} P(A_i)\,P(B/A_i). \tag{7.58}$$

* * * * * * * * * *

UCLA STANDARD PROCEDURE 1110.1 - ATTACHMENT A

University of California, Los Angeles
Campus Veterinarian, IV-211 C.H.S.
Telephone: (213) 825-6240

Office Use Only
Application # 33-76 C Project ID #
Effective 6-1-80 Expiration 5-31-84 5-31-85

APPLICATION FOR USE OF LABORATORY ANIMAL SUBJECTS

A separate application must be completed and typewritten for each proposed project or activity utilizing animals.* Applications should be directed to the Campus Veterinarian for review, but can be sent after funding agency deadlines. However, an approved application is required for the University to accept extramural funds and before any animals can be ordered.

Applicant Charles D. Woody, MD

Phone: Office 825-0187 Home

Department/Division NPI/MR

Title of Research or Training Project/Activity Neurophysiological Research Supporting the Investigation of Adaptive Network Architectures

Estimated Starting Date 6/1/80 Estimated Completion Date 5/31/84 5/31/85

The undersigned attests to the attached information, and agrees to accept responsibility that all animal use in the above-titled project or activity will be in accordance with University, Federal, and other relevant policies and regulations. Any changes will be communicated to the Chancellor's Committee/Campus Veterinarian.

Signature Charles D. Woody 5/23/80
(Title) (Date)
Charles D. Woody, MD Professor of Anatomy and Psychiatry

*"Animal" *means any live or dead vertebrate.*

For Committee Use Only

☑ Application Approved: Effective Date 6-1-80 Expiration Date 5-31-84 5-31-85 ☐ Application Disapproved

Comments:

Signature [signature] 6-2-80
(Title) (Date)

UCLA STANDARD PROCEDURE 1110.1 - ATTACHMENT A

University of California, Los Angeles
Campus Veterinarian, IV-211 C.H.S.
Telephone: (213) 825-6240

Office Use Only
Application # 33-764 Project ID #
Effective 6-1-80 Expiration 5-31-84

APPLICATION FOR USE OF LABORATORY ANIMAL SUBJECTS

1. Applicant Charles D. Woody, MD Department NPI/MR
Phone: Office 825-0187 Home

2. Contact for animal problems & emergencies Charles D. Woody, MD
Phone: Office 825-0187 Home

3. Title of research or training project/activity Neurophysiological Research Supporting the Investigation of Adaptive Network Architecures

4. Starting Date 6/1/80 to 5/31/84 ☐ New ☒ Continuation ☐ Renewal ☐ Supplemental

5. ☒ Extramural funding, Acad. Senate, or Cal. Inst. for Cancer Res.: *Attach copy of proposal application.*

6. ☐ Intramural or other funding: *On cont. page outline project's objectives, animal purchasing & care budget.*

7. Animal Use Sites – building(s)/room(s) 58-147, 58-159, 57-384.

8. For animals held in laboratory more than 12 hours, does housing conform to DHEW Guide: ☒ Yes ☐ No

9. Species/Strain/Breed Cat Sex ___ Age/Weight Range

10. Total number for entire project/activity 20-40 per annum Expected Daily Population 12

11. ☐ Special procurement or processing needs: *Specify on continuation page.*

12. ☐ Procurement of dead animal material: *Answer questions 1-12 only and sign application.*

13. ☐ Short term use (up to 2 weeks) ☐ Long term use (more than 2 weeks) ☒ Both ☐ Breeding program

14. ☒ Standard housing, diet, sanitation & pest control ☐ Special needs: *Specify on continuation page.*

15. ☐ Project involves no pain or distress to animal subjects. *Refer to "Guiding Principles" #5.*

16. ☒ Project involves probable pain or distress to animal subjects. *Details of procedures on animals presented in:* ☐ *proposal application* ☐ *continuation page* ☐ *attached journal reprint*

17. ☒ Pain or distress relieved by anesthetic, analgesics, tranquilizers. *Use cont. page for add'l drugs.*
Cite: Drug(s) NA Pentobarbital Dosage 50mgm/kg Route IP

18. ☐ Pain or distress cannot be relieved. *Explain basis for exception on continuation page.*

19. ☐ Surgery: ☐ Nonsurvival ☒ Survival ☒ Aseptic Surgery ☐ Multiple surgeries on same animal

20. Procedure for sick/dead animals: ☐ Veterinary attention ☐ Discard ☒ Notify applicant

21. ☒ Euthanasia: Cite: drug(s) Nembutal Route IP
Cite other method(s)

22. ☐ Special veterinary & technical services required: *Specify on continuation page.*

23. ☐ Potential biological or radiation hazard to: ☐ Humans ☐ Animals *Describe on continuation page.*

USE CONTINUATION PAGE(S) FOR ADDITIONAL INFORMATION